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Via Electronic Submission

December 6, 2001

Hon. Christine Todd Whitman
US Environmental Protection Agency
PO Box 1473
Merrifield, VA 22116

Attn: Chemical Right-to-Know Program

ExxonMobil Chemical Company Registration Number

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Dear Ms. Whitman:

ExxonMobil Chemical Company (EMCC) submits for review and public comment the test plan and related robust summaries for the *Neo Acids C5-C28* category, under the US High Production Volume (HPV) Chemical Challenge program, AR-201. The test plan and robust summary files are provided electronically in the attached zip file in Word 95/97 format.

This test plan covers the following category of chemicals, Neo Acids C5-C28:

- CAS# 75-98-9: Propanoic acid, 2,2-dimethyl-
- CAS# 598-98-1: Propanoic acid, 2,2-dimethyl-, methyl ester
- CAS# 95823-36-2: Carboxylic acid, C6-8 neo
- CAS# 26896-20-8: 2,2-Dimethyloctanoic acid
- CAS# 68938-07-8: Fatty acids, C9-C13 neo
- CAS# 72480-45-6: Fatty acids, C9-C28 neo

We understand that this information will be posted on the internet for a 120 day comment period. Please forward technical comments on this test plan to Laura H. Keller at the above address or you may contact her at (281) 870-6501 (email: laura.h.keller@exxonmobil.com).

Please note that EMCC's corporate contact for future questions from the U.S. EPA about the HPV Challenge Program has been changed from Mr. Gailen A. Hart to:

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Sincerely,

Nigel J. Sarginson
Product Stewardship & Regulatory Affairs Manager
ExxonMobil Chemical Company

2001 DEC - 7 AM 9:38

HIGH PRODUCTION VOLUME (HPV)
CHEMICAL CHALLENGE PROGRAM

TEST PLAN

For The

NEOACIDS C5-C28 CATEGORY

CAS# 75-98-9: Propanoic acid, 2,2-dimethyl-
CAS# 598-98-1: Propanoic acid, 2,2-dimethyl-, methyl ester
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CAS# 26896-20-8: 2,2-Dimethyloctanoic acid
CAS# 68938-07-8: Fatty acids, C9-C13 neo
CAS# 72480-45-6: Fatty acids, C9-C28 neo

Prepared by:

ExxonMobil Chemical Company

November 15, 2001

EXECUTIVE SUMMARY

Under EPA's High Production Volume (HPV) Challenge Program ExxonMobil Chemical Company has committed to voluntarily compile a Screening Information Data Set (SIDS) on a category of chemicals defined as Neoacids C5-C28. This category is supported by the basic screening data needed for an initial assessment of the

of chemicals as defined by the Organization for Economic Cooperation and Development (OECD). The information used to complete the HPV SIDS endpoints comes from existing data.

ExxonMobil Chemical Company believes a category of Neoacids C5-C28 is scientifically justifiable because their physicochemical and toxicological properties are very similar and follow a regular pattern as a result of the synthesis process. The structural similarities create a predictable pattern in the following parameters: physicochemical properties, environmental fate and effects, and human health effects. The similarities are based on the following:

- A common structure represented by R3CCOH,
- An incremental and constant change in carbon number across the category where the total number of carbons represented by R ranges from 3 to 26, and
- A likelihood of common precursors and breakdown products that can result in structurally similar metabolites (e.g. carboxylic acid).

This test plan is based on the observation that the toxicological properties are similar or vary in an incremental and predictable fashion within the category.

The test data compiled for the category anchor studies proves adequate to support a screening-level hazard assessment for the category and its members (CAS numbers, 75-98-9, 598-98-2, 95823-36-2, 26896-20-8, 68938-07-8, and 72480-45-6). The untested endpoints can be assessed by interpolation between data from the category anchor studies.

To complete the hazard assessment of the category, Ames, micronucleus, and algal toxicity studies will be completed on both low and high molecular weight members of the category (75-98-9 and 72480-45-6 or 68938-07-8). Also, a fish acute and invertebrate toxicity study will be conducted on a high molecular weight member (68938-07-8).

Evaluation of the Neoacids C5-C28 as a category has several advantages. The category can be evaluated by using a matrix of completed anchor studies for various members of the category. By using this approach, the safety of the category can be determined without having to conduct tests for every end-point with every chemical. Not only will this inform the public earlier about any hazards of Neoacids C5-C28, but it will also reduce the number of animals that would be required to evaluate the toxicity of individual members of the Neoacids C5-C28 category.

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TEST PLAN FOR NEOACIDS C₅-C₂₈

I. INTRODUCTION

Under EPA's High Production Volume (HPV) Chemical Challenge Program ExxonMobil Chemical Company has committed to voluntarily compile a Screening Information Data Set (SIDS) on a category of chemicals defined as Neoacids C5-C28. This category is supported by the basic screening data needed for an initial assessment of the physicochemical properties, environmental fate, and human and environmental effects of chemicals as defined by the Organization for Economic Cooperation and Development (OECD). The information used to complete the HPV SIDS endpoints comes from existing data and fulfills an ExxonMobil obligation to the HPV Challenge Program.

ExxonMobil Chemical Company believes a category of Neoacids C5-C28 is scientifically justifiable because their physicochemical and toxicological properties are very similar and follow a regular pattern as a result of the synthesis process. The structural similarity of the component chemicals from these products creates a predictable pattern in the following parameters: physicochemical properties, environmental fate and effects, and human health effects. The similarities are based on the following:

- A common structure represented by R3CCOH,
- An incremental and constant change in carbon number across the category where the total number of carbons represented by R ranges from 3 to 26, and
- A likelihood of common precursors and breakdown products that can result in structurally similar metabolites (e.g. carboxylic acid).

This test plan is based on the observation that the toxicological properties are similar or vary in an incremental, predictable fashion within the category.

The test data compiled for the category proves adequate to support a hazard assessment for the category and its members (CAS numbers, 75-98-9, 598-98-2, 95823-36-2, 26896-20-8, 68938-07-8, and 72480-45-6) with the exception of few studies that have been identified as necessary to complete a thorough hazard dataset. Once all data are available, the untested endpoints can be assessed by interpolation between data from the category anchor studies. The existing data suggest that products in the Neoacids (C₅-C₂₈) Category exhibit relatively low toxicity for human health endpoints and moderate toxicity for the environmental health endpoints.

To complete the hazard assessment of the category, Ames, micronucleus, and algal toxicity studies will be completed on the low and high molecular weight members of the category (75-98-9 and 72480-45-6 or 68938-07-8). Also, a fish acute and invertebrate toxicity study will be conducted on a high molecular weight member (68938-07-8).

The data from this category will be used to inform the public about the potential hazards of the Neoacids C5-C28. Developing a data matrix of anchor studies and applying justifiable read across practices will provide a sufficiently robust data set to characterize each endpoint in the HPV Chemical Challenge Program without having to conduct a test

for each endpoint and product. This resourceful use of existing data will result in fewer animals needed for testing purposes while adequately assessing the potential hazards of products in the Neoacids C5-C28 Category.

II. CHEMICAL PROCESS AND DESCRIPTION

The Neoacids C5-C28 Category contains a group of neoacid products whose physicochemical and toxicological properties are very similar and follow a regular pattern as a result of synthesis and structural similarity (Table 1). The production of neoacid products involves the reaction between a branched olefin with carbon monoxide and water at elevated temperatures and pressures in the presence of an acid catalyst.

The category also contains propanoic acid, 2,2-dimethyl-, methyl ester (CAS#: 598-98-1). This material is an ester that is rapidly hydrolyzed to the parent neoacid - propanoic acid, 2,2-dimethyl- (CAS#: 75-98-9). Because of this rapid hydrolysis, propanoic acid, 2,2-dimethyl-, methyl ester has properties for health effects, aquatic toxicity, and environmental fate that are consistent with the neoacids.

The structural similarity of chemicals in this category creates a predictable pattern in the following parameters: physicochemical properties, environmental fate and effects, and human health effects. Neoacids are trialkylacetic acids in which each hydrogen on the non carboxyl carbon of acetic acid has been replaced by an alkyl group. The structural features of members of the category are as follows:

- A common structure - a quaternary carbon with the general structure R_3CCOOH ,
- An incremental and constant change across the category where R can be a branched alkyl group ranging from CH_3 to C_6H_{13} as the main constituent,
- A likelihood of common precursors and breakdown products which result in structurally similar chemicals.

Table 1. CAS Numbers and Descriptions

CAS Number	Chemical Name
75-98-9	Propanoic acid, 2,2-dimethyl-
598-98-1	Propanoic acid, 2,2-dimethyl-, methyl ester
95823-36-2	Carboxylic acid, C6-8 neo*
26896-20-8	2,2-Dimethyloctanoic acid
68938-07-8	Fatty acids, C9-13 neo
72480-45-6	Fatty acids, C9-28 neo

* = Not currently HPV but included to facilitate category evaluation

The Neoacids C5-C28 category accomplishes the goal of the Challenge Program - to obtain screening level hazard information through the strategic selection of products to be tested within the category. The testing strategy is based on the principle that:

- These products behave in a similar or predictable manner, and
- Interpolation of data can be used to assess the neoacid products for which data are not available.

Procedures to assess the reliability of selected data for inclusion in this test plan are based on the guidelines described by Klimisch et al, 1997.

III. TEST PLAN RATIONALE

A. Physicochemical Data

Physicochemical Data (i.e., melting point, boiling point, vapor pressure, water solubility, and Kow) for selected chemical components in the Neo Acid C5 - C28 Category will be calculated using EPIWIN® model (EPIWIN, 1999), as discussed in the EPA document entitled "The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program." These data will be presented as ranges, based on the chemical components selected to represent each neoacid product. In addition, measured data for some of these endpoints will also be provided for selected neoacid products where readily available. Where possible, measured and calculated data will be presented together for comparison purposes.

Table 2 lists selected measured physicochemical data (melting point, boiling point, and vapor pressure) as they appear on the material safety data sheets for products in this category. These data are provided with this test plan to further justify these products as a distinct category under the HPV Chemical Challenge Program. Also included are calculated values for water solubility and K_{ow}. As shown by the data in Table 2, the structural similarity of the neoacid products results in a predictable and incrementally increasing pattern of physiochemical properties from the C5 to C9-28 products.

Table 2. Selected Physical Properties of Neoacids (C₅-C₂₈)

CAS NUMBER	CHEMICAL NAME	MELTING POINT (° C)	BOILING POINT (° C)	WATER SOLUBILITY mg/L	VAPOR PRESSURE (mm Hg @ 20° C)	Log Kow
75-98-9	Propanoic acid, 2,2-dimethyl- (C5)	9.87	166.9	15,590	1.54	1.5
598-98-1	Propanoic acid, 2,2-dimethyl-, methyl ester (C6)	21.6	187.8	6,135	0.721	1.94
95823-36-2	Carboxylic acid, C6-8 neo (C7)	37.4	207.8	1,537	0.117	2.5
26896-20-8	2,2-Dimethyloctanoic acid (C10)	48.1	252.1	80	0.0147	3.8
68938-07-8	Fatty acids, C9-13 neo	37 - 76	234 - 291	3.1 - 243	0.001 - 0.046	3.3 - 5.2
72480-45-6	Fatty acids, C9-28 neo	37 - 204	234 - 504	<1 - 243	<1.7 E ⁻¹² - 0.046	3.3 - 6.0

B. Human Health Effects

The structural similarity of the Neoacids C5-C28 influences both their physicochemical (Table 2) and their toxicological properties (Sections C and D). As a chemical category, the Neoacids C5-C28 have predictable, low-level environmental and health hazards.

ExxonMobil Chemical Company believes the category of Neoacids C5-C28 is scientifically justifiable and that the test data compiled for the category proves adequate to support a screening-level hazard assessment for the category and its members (CAS numbers, 75-98-9, 598-98-2, 95823-36-2, 26896-20-8, 68938-07-8, and 72480-45-6). One can assess the untested endpoints by extrapolation between and among the category members. The proposed category assessment plan is shown in Table 3.

Metabolism

Propanoic acid, 2,2-dimethyl-, methyl ester is rapidly cleaved to Propanoic acid, 2,2-dimethyl-. Due to the stability conferred by the quaternary carbon, Neoacids C5-C28 are relatively resistant to biotransformation and do not readily form bioactive metabolites. Enzymatic removal of the alkyl groups at the quaternary carbon would allow for other metabolic processes to occur. These would likely be mitochondrial beta-oxidation or by cytochrome P450 mediated omega and omega-minus-one oxidation (may be followed by beta-oxidation) to produce acetate. However, since Neoacids C5-C28 are not readily metabolized, they would primarily be eliminated in the urine as glucuronic acid conjugates or by dealkylation (Katz and Guest, 1994).

C. Presentation of Neoacids C5-C28 Category Health Effects Data Associated with the Anchor Studies under the HPV Challenge Program

Acute Oral Toxicity

TEST	Propanoic acid, 2,2-dimethyl- (C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C6)	Carboxylic acid, C6-8 neo (C7)	2,2-Dimethyloctanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
ACUTE ORAL - RAT	= 2000 mg/kg	RA	1860 mg/kg	= 2000 mg/kg	RA	RA

All of the Neoacids C5-C28 have a low order of toxicity to rats via the oral route of exposure (EBSI, 1964). The LD₅₀ values for Propanoic acid, 2,2-dimethyl- and 2,2-Dimethyloctanoic acid were 2000 mg/kg. In addition, the LD₅₀ for Carboxylic acid, C6-8 neo was 1860 mg/kg. These results demonstrate that members of the Neoacids C5-C28 Category have a consistent, low order of acute oral toxicity.

Acute Dermal Toxicity

TEST	Propanoic acid, 2,2-dimethyl- (C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C6)	Carboxylic acid, C6-8 neo (C7)	2,2-Dimethyl-ctanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
ACUTE DERMAL - RABBIT	= 3160 mg/kg	RA	> 3160 mg/kg	> 3160 mg/kg	RA	RA

The Neoacids C5-C28 have a low order of toxicity via the dermal route of exposure (EBSI, 1964). The rabbit dermal LD₅₀ for all members of the category was equal to or greater than 3160 mg/kg. This indicates that the members of this category have a consistent pattern of acute toxicity via the dermal route of exposure.

Genotoxicity

TEST	Propanoic acid, 2,2-dimethyl- (C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C6)	Carboxylic acid, C6-8 neo (C7)	2,2-Dimethyl-ctanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
AMES - <i>S. typhimurium</i> ; TA98, 100, 1535, 1537, 1538 ± Activation	T	RA	RA	RA	RA	T
Chromosomal Aberration - In Vitro or In Vivo	T	RA	RA	RA	RA	T

RA Read Across
T Test Proposed

There are no structural alerts to suggest that Neoacids C5-C28 are likely to be genotoxic. However, because there are no data available to assess the genotoxic potential of Neoacids C5-C28, we propose to conduct tests to evaluate this endpoint. First, Ames tests will be conducted on materials at either end of the category (Propanoic acid, 2,2-dimethyl- and Fatty acids, C9-28 neo) to evaluate the mutagenicity of the category. Second, mouse micronucleus tests will be conducted on these same materials to evaluate the clastogenicity of the category. The mouse micronucleus test is widely accepted by regulatory agencies to evaluate clastogenicity. This category approach will minimize the amount of unnecessary animal testing and will maximize the utility of both existing and newly generated data.

Subchronic Toxicity

TEST	Propanoic acid, 2,2-dimethyl- (C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C6)	Carboxylic acid, C6-8 neo (C7)	2,2-Dimethyloctanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
RAT DERMAL	NOAEL (dermal) = 300 mg/kg	RA	NOAEL (dermal) = 553.7 mg/kg	NOAEL (dermal) = 2280 mg/kg	RA	RA

The subchronic toxicity of Neoacids C5-C28 has been assessed by conducting repeat dermal exposure studies. Dermal exposure is the primary route of exposure for Neoacids C5-C28, particularly in an industrial setting. An evaluation of the repeated dose studies indicates that Neoacids C5-C28 have a low order of subchronic toxicity. Propanoic acid, 2,2-dimethyl-, in isopropyl alcohol solution, was repeatedly applied to the shaved intact skin of albino rabbits 5 days/week for two weeks (for a total of 10 applications) at doses of 30 or 300 mg/kg/day (Hazleton, 1964a). Slight to moderate irritation at the low dose and moderate to marked irritation at the high dose was observed. Slight or moderate erythema, atonia, and desquamation were seen at the low dose. At the high dose, skin irritation consisted of moderate erythema, slight to marked edema, moderate or marked atonia and desquamation. Some dermal necrosis at the site of application was seen in three rabbits and persisted throughout the study. Control animals that received only the solvent (isopropyl alcohol) showed slight irritation. There were no signs of systemic toxicity attributable to dermal absorption of propanoic acid, 2,2-dimethyl-. The NOAEL for systemic toxicity in this study was 300 mg/kg.

In a similar study, carboxylic acid, C6-8 neo was applied at 55.4 mg/kg and 553.7 mg/kg for 10 applications (Hazleton, 1964b). No treatment related effects were observed on behavior of clinical signs during the in-life phase of the study. Gross pathology of the animals in all dose groups did not reveal any abnormalities. Repeated application of carboxylic acid C6-8 neo did produce marked skin irritation with some dermal necrosis at the site of application in the high dose group. Since no systemic effects were observed in this study, the NOAEL for systemic effects following subchronic dermal application of carboxylic acid, C6-8 neo was 553.7 mg/kg.

Repeated dermal application (400 or 2800 mg/kg daily for a total of 10 applications) of undiluted 2,2-dimethyloctanoic acid generally produced irritation at the low dose and fissuring at the high dose (Hazleton, 1964c). Slight to moderate erythema, atonia and desquamation were seen at the low dose. At the high dose, skin irritation consisted of moderate erythema, moderate to severe atonia, and desquamation with fissuring. No signs of systemic toxicity were attributed to 2,2-dimethyloctanoic acid. Therefore, the NOAEL for systemic toxicity following subchronic dermal application of 2,2-dimethyloctanoic acid was 2280 mg/kg.

In summary, Neoacids C5-C28 have a low order of subchronic toxicity. In addition, they display a consistent pattern of subchronic toxicity in that the NOAEL for systemic toxicity increases in a predictable pattern from the low to the high molecular weight end of the

category. Therefore, Neoacids C5-C28 do not require further testing to assess subchronic toxicity.

Developmental Toxicity

TEST	Propanoic acid, 2,2-dimethyl- (C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C6)	Carboxylic acid, C6-8 neo (C7)	2,2-Dimethyloctanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
DEVELOPMENTAL ORAL - RAT	RA	RA	NOAEL maternal = 250 mg/kg NOAEL fetal = 250 mg/kg NOAEL (isooctanoic) maternal = 400 mg/kg NOAEL fetal = 800 mg/kg NOAEL (isooctanoic acid) = 7500 ppm in diet	NOAEL parental = 1500 ppm in diet NOAEL F1 = 1500 ppm NOAEL F2 = 1500 ppm	NOAEL (isononanoic acid) = 1200 ppm in diet	RA

The potential for developmental toxicity of Neoacids C5-C28 can be assessed by evaluating the available data on neoacids as well as by comparison to the data on isoacids and structure-teratogenicity relationships. The available developmental toxicity data on neoacids indicate that they are not selective developmental toxicants. A developmental toxicity study conducted on Carboxylic acid, C6-8 neo produced a NOAEL of 250 mg/kg for both maternal and fetal effects (EBSI, 1986). Carboxylic acid, C6-8 neo was not a selective developmental toxicant in this study. In a 3-generation reproduction study with 2,2-Dimethyloctanoic acid, developmental effects were not observed in either the F1 or F2 offspring (EBSI, 1968). This study produced a NOAEL of 1500 ppm (in diet) for the maternal, F1, and F2 generations.

Additional developmental toxicology data are available for isoacids, which are isomers of the neoacids. The isoacids are aliphatic carboxylic acids that have saturated branching structures. Isooctanoic acid was tested for developmental toxicity in female rats at doses of 0, 200, 400, and 800 mg/kg/day during gestation days 6 - 15 (EBSI, 1995). At 800 mg/kg/day, maternal toxicity was observed; however, there were no effects at 400 mg/kg/day. There were no biologically significant developmental effects in this study. The no-observable-adverse-effect level (NOAEL) for maternal toxicity was 400 mg/kg/day and for developmental toxicity was 800 mg/kg/day.

In a one-generation reproductive toxicity range-finding study, rats were exposed to isooctanoic acid at dietary levels of 1000, 5000, 75000, or 10,000 ppm (EBSI, 1999). In the parental generation, there were no treatment-related effects on survival, organ weights, or reproductive function. In the offspring, there were no treatment-related

effects on survival, developmental landmarks, or any significant findings in postmortem evaluations. Statistically significant decreases in the mean offspring body weights of males and females were observed at 10,000 ppm. The high dose also resulted in a suppression of body weight gain in the adult females. Thus, the NOAEL for both parental and offspring effects was 7500 ppm.

A one-generation reproduction study was conducted on isononanoic acid (EBSI, 1998). Rats were administered the test material in the diet at doses of 0, 600, 1200, 2500, and 5000 ppm. There were no treatment-related effects observed on mating, fertility, fecundity, or gestation indices or during sperm analysis. Evidence of maternal toxicity included decreased body weights and increased liver weights in the 2500 and 5000 ppm dose groups. In the offspring, reduced survival indices were noted in the 5000 ppm dose group, and reduced body weights were noted in the 2500 and 5000 ppm dose groups. The NOAEL for both maternal and offspring effects in this study was 1200 ppm.

Further support for the evaluation of the potential of neoacids to be developmental toxicants comes from an analysis of the structure activity relationships that affect teratogenicity. A structure-teratogenicity analysis of carboxylic acids concluded that aliphatic acids, which have a dimethyl substitution at the C-2 position, are not developmental toxicants (Di Carlo, 1990). Furthermore, the structural requirements for carboxylic acid teratogenicity require an alpha hydrogen and a free carboxylic group. Since the neoacids are defined by their trialkyl substitution at the alpha carbon, there is no alpha hydrogen. In addition, steric hindrance of the carbonyl group by the quaternary center of the alpha carbon inhibits reactions.

In conclusion, the available test data on neoacids and their isomers, as well as the structure-teratogenicity relationship for aliphatic acids, provide sufficient information for a screening-level assessment of the developmental toxicity of neoacids. Based on these analyses, neoacids are not considered to be selective developmental toxicants and no further testing is proposed.

Reproductive Toxicity

TEST	Propanoic acid, 2,2-dimethyl- (C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C6)	Carboxylic acid, C6-8 neo (C7)	2,2-Dimethyl-ctanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
REPRODUCTIVE ORAL - RAT	RA	RA	NOAEL (isooctanoic acid) = 7500 ppm in diet	NOAEL parental = 1500 ppm in diet NOAEL F1 = 1500 ppm NOAEL F2 = 1500 ppm	NOAEL (isononanoic acid) = 1200 ppm in diet	RA

The available reproductive toxicity studies and developmental toxicity studies prove adequate to support a screening-level hazard assessment for the reproductive toxicity

potential of Neoacids C5-C28. These data support the conclusion that the Neoacids C5-C28 are not selective reproductive toxicants.

In a modified three-generation reproduction study, rats were exposed to 100, 500, or 1500 ppm 2,2-dimethyloctanoic acid in the diet (approximately 5, 25 and 75 mg/kg/day, respectively) (EBSI, 1968). No significant effects were observed in survival, appearance, behavior, or reproductive performance of the parents. No adverse effects were demonstrated in offspring on growth, appearance, or behavior. No treatment related effects were observed at gross or microscopic pathology. The NOAEL in this study was greater than 1500 ppm. The data indicate that 2,2-dimethyloctanoic acid is not a reproductive toxicant.

In a one-generation reproductive toxicity range-finding study, rats were exposed to isooctanoic acid at dietary levels of 1000, 5000, 75000, or 10,000 ppm (EBSI, 1999). In the parental generation, there were no treatment-related effects on survival, organ weights, reproductive function, or sperm indices. In the offspring, there were no treatment-related effects on survival, developmental landmarks, or any significant findings in postmortem evaluations. Statistically significant decreases in the mean offspring body weights of males and females were observed at 10,000 ppm. The high dose also resulted in a suppression of body weight gain in the adult females. Thus, the NOAEL for both parental and offspring effects was 7500 ppm.

A one-generation reproduction study was also conducted on isononanoic acid (EBSI, 1998). Rats were administered the test material in the diet at doses of 0, 600, 1200, 2500, and 5000 ppm. There were no treatment-related effects observed on mating, fertility, fecundity, or gestation indices or during sperm analysis. Evidence of maternal toxicity included decreased body weights and increased liver weights in the 2500 and 5000 ppm dose groups. In the offspring, reduced survival indices were noted in the 5000 ppm dose group, and reduced body weights were noted in the 2500 and 5000 ppm dose groups. The NOAEL for both maternal and offspring effects in this study was 1200 ppm.

In summary, these data prove adequate to support a screening level assessment of the reproductive toxicity of Neoacids C5-C28. Furthermore, these data indicate that Neoacids C5-C28 have a low order of reproductive toxicity.

D. Aquatic Toxicity

The neoacid products ranging from Propanoic acid, 2,2-dimethyl- to fatty acids, C9-13 neo, have been shown to produce an expected increasing level of acute toxicity to freshwater fish and invertebrates. This is based on data from the literature that are used to read across to selected neoacid products in this test plan and company data specifically for products in this category. Although there are insufficient data to confirm that a similar pattern of alga toxicity exists, based on the fish and invertebrate data, a similar increasing level of toxicity is expected from the lower to higher carbon numbered products. Proposed testing will develop the data needed to confirm this expectation. Based on the existing data, products in the Neoacids (C₅-C₂₈) Category demonstrate a

low to moderate degree of aquatic toxicity from the low to high carbon numbered products, respectively.

Fish Acute Toxicity

TEST	Propanoic acid, 2,2-dimethyl- (C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C6)	Carboxylic acid, C6-8 neo (C6-8)	2,2-Dimethyl-octanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
FISH ACUTE TOXICITY (96-hour, mg/L)	380	RA	630*	37.2	TESTING PROPOSED	RA

RA read across * Data are for a C7 branched and linear aliphatic acid product that does not contain a quaternary carbon, but is used to read across to a C6-8 neoacid product

Acute experimental fish toxicity tests are reported for Rainbow Trout (*Oncorhynchus mykiss*) and Goldfish (*Carassius auratus*). The results show that a C5 neo acid, C7 linear and branched aliphatic acid (used as read across to the C6-8 neo acid), and C10 neo acid products demonstrate that these products have a potential to cause acute fish toxicity (96-hour LC50) in the range of 630 to 37.2 mg/L.(Bridie 1979, EBSI 1993c, EBSI 1996b). The C9-13 neoacid, and the C9-28 neoacid products are not characterized. Therefore, to adequately assess the potential toxicity of the Neoacids (C₅-C₂₈) Category to fish, an acute toxicity test with the fatty acids, C9-13, neo, product will be conducted. The data from this study will be used to read across to the fatty acids, C9-28, neo, product. Comparable toxicity is expected for these two products because the higher molecular weight fatty acid components in the C9-28 neo acid product have extremely low water solubilities and do not have the potential to be in solution at effect causing levels, unlike the lower molecular weight components whose water solubilities are sufficient to cause an effect as demonstrated by the C10 neoacid product.

Invertebrate Acute Toxicity

TEST	Propanoic acid, 2,2-dimethyl- (C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C6)	Carboxylic acid, C6-8 neo (C7)	2,2-Dimethyloctanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
DAPHNID ACUTE TOXICITY (48-hour, mg/L)	203	RA	138	47.1	TESTING PROPOSED	RA

RA read across

Acute experimental toxicity studies are reported for the Daphnid (*Daphnia magna*). The results show that a C5 neo acid, C7 linear and branched aliphatic acid (used as read across to the C6-8 neo acid), and C10 neo acid product have the potential to cause

acute toxicity (48 hour EL50 or EC50) in the range of 203 to 47.1 mg/L (EG&G 1977a, EG&G 1977b, EBSI 1993a). The C9-13 neoacid, and the C9-28 neoacid products are not characterized. Therefore, to adequately assess the potential toxicity of the Neoacids (C₅-C₂₈) Category to the Daphnid, an acute toxicity test with the fatty acids, C9-13, neo, product will be conducted. The data from this study will be used to read across to the fatty acids, C9-28, neo, product. Comparable toxicity is expected for these two products because the higher molecular weight fatty acid components in the C9-28 neo acid product have extremely low water solubilities and do not have the potential to be in solution at effect causing levels, unlike the lower molecular weight components whose water solubilities are sufficient to cause an effect as demonstrated by fish and invertebrate toxicity data for the C10 neoacid product.

Alga Toxicity

TEST	Propanoic acid, 2,2-dimethyl- (C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C7)	Carboxylic acid, C6-8 neo (C6-8)	2,2-Dimethyl-octanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
ALGA TOXICITY (96-hour, mg/L)	TESTING PROPOSED	RA	6.5 (2)	RA	TESTING PROPOSED	RA

(1) biomass
(2) growth rate
RA read across

An acute experimental toxicity value is reported for the freshwater alga (*Selenastrum capricornutum*) for a C7 linear and branched aliphatic acid product that is used as read across data to the C7 neoacid. This result shows that a C7 acid product has the potential to cause toxicity (72 hour EC50) at a concentration of 6.5 mg/L, based on alga growth rate (EBSI 1993b). Although there are no data for the remaining neoacid and neoacid ester products, overall, they are expected to exhibit a range of toxicity that falls above and below the value for the C7 aliphatic acid product. To adequately assess the potential toxicity of the Neoacids (C₅-C₂₈) Category to an alga, toxicity tests with a C5 neoacid and fatty acids, C9-13, neo, product will be conducted. The data from the fatty acids, C9-13, neo, product will be used to read across to the fatty acids, C9-28, neo, product. Comparable toxicity is expected for these two products because the higher molecular weight fatty acid components in the C9-28 neo acid product have extremely low water solubilities and do not have the potential to be in solution at effect causing levels, unlike the lower molecular weight components whose water solubilities are sufficient to cause an effect as demonstrated by the C10 neoacid product.

E. Environmental Fate

Biodegradation data are available for three neoacid products. They show that neoacid products do not have the potential to biodegrade to a great extent within a standard 28-day test duration.

Although there is some information on photodegradation and fugacity, a complete data set to adequately characterize the neoacid products does not exist. Chemical equilibrium models are used to calculate fugacity, which describes the potential of a chemical to partition in the environment. These data can only be calculated. Preliminary information for selected component chemicals of products in the Neoacids (C₅-C₂₈) Category suggests that these products are expected to partition primarily to water and soil. However, their fate in air is of environmental interest (this is discussed below under photodegradation). In addition, the majority of the component chemicals in these products have relatively low K_{ow} values, which suggests that they will not tend to partition to suspended organic matter in air and precipitate to aquatic and terrestrial environmental compartments to a significant extent.

Biodegradation

TEST	Propanoic acid, 2,2-dimethyl- (C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C6)	Carboxylic acid, C6-8 neo (C6-8)	2,2-Dimethyloctanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
28-Day Aerobic Biodegradation Test	24.1 %ThOD	RA	44.0 %ThOD	11 % ThOD	2.3 % ThOD	RA

RA read across

* data developed using an acclimated inoculum

The existing biodegradation data for the neoacids products suggest that these products will not degrade rapidly in the environment. Four products have been tested and they exhibited an extent of biodegradation that ranged from approximately 2 to 44% after 28 days incubation (EBSI 1996a). These data were generated using a closed system with non-acclimated inocula. The test systems were continuously stirred, which is recommended when evaluating mixtures with several components, some of which have minimal water solubility.

Photodegradation – Photolysis

Direct photochemical degradation occurs through the absorbance of solar radiation by a chemical substance. If the absorbed energy is high enough, then the resultant excited state of the chemical may undergo a transformation. Simple chemical structures can be examined to determine whether a chemical has the potential for direct photolysis in water. First order reaction rates can be calculated for some chemicals that have a potential for direct photolysis using the procedures of Zepp and Cline (Zepp, 1977). UV light absorption of the chemical components in this category will be evaluated to identify those having the potential to degrade in solution. For those compounds with a potential for direct photolysis in water, first order reaction rates will be calculated. A technical document will be prepared that summarizes the results of information developed for this endpoint.

Photodegradation – Atmospheric Oxidation

Photodegradation can be measured (US EPA, 1999a) (EPA identifies OECD test guideline 113 as a test method) or estimated using models accepted by the EPA (US EPA, 1999b). An estimation method accepted by the EPA includes the calculation of atmospheric oxidation potential (AOP).

Atmospheric oxidation as a result of hydroxyl radical attack (OH \cdot) is not direct photochemical degradation, but rather indirect degradation. AOPs can be calculated using a computer model. Neoacid products, such as those in the Neoacid (C₅-C₂₈) Category, have a lower potential to volatilize to air. In air, these chemicals may undergo reaction with photosensitized oxygen in the form of ozone and hydroxyl radicals.

The computer program AOPWIN (atmospheric oxidation program for Microsoft Windows) (EPIWIN, 1999) is used by OPPTS (Office of Pollution Prevention and Toxic Substances). This program calculates a chemical half-life based on an overall OH \cdot -reaction rate constant, a 12-hr day, and a given OH \cdot -concentration. This calculation will be performed for the representative chemical components in the Neoacids (C₅-C₂₈) Category and summarized in robust summaries for this group of products.

Stability in Water (Hydrolysis)

Hydrolysis of an organic chemical is the transformation process in which a water molecule or hydroxide ion reacts to form a new carbon-oxygen bond. Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (Neely, 1985). Stability in water can be measured (US EPA, 1999a) (EPA identifies OECD test guideline 111 as a test method) or estimated using models accepted by the EPA (US EPA, 1999b).

All of the chemical structures included in this category are neoacids with the exception of propanoic acid, 2,2-dimethyl-, methyl ester (C₆ neoacid methyl ester), which is a carboxylic acid ester. The neoacid products are not expected to hydrolyze at a measurable rate. A technical document will be prepared that discusses the nature of the chemical bonds present and the potential reactivity of this group of chemicals with water. The computer model Hydrowin version 1.67 (EPIWIN 1999) will be used to calculate the potential hydrolysis rate for the C₆ neoacid methyl ester. This information will be summarized in robust summaries for this group of products.

Chemical Transport and Distribution In The Environment (Fugacity Modeling)

Fugacity based multimedia modeling can provide basic information on the relative distribution of chemicals between selected environmental compartments (i.e., air, soil, sediment, suspended sediment, water, biota). The US EPA has acknowledged that computer modeling techniques are an appropriate approach to estimating chemical

partitioning (fugacity is a calculated endpoint and is not measured). A widely used fugacity model is the EQC (Equilibrium Criterion) model (Mackay, 1996). EPA cites the use of this model in its document titled *Determining the Adequacy of Existing Data* (US EPA, 1999a), which was prepared as guidance for the HPV Program.

In its document, EPA states that it accepts Level I fugacity data as an estimate of chemical distribution values. The input data required to run a Level I model include basic physicochemical parameters; distribution is calculated as percent of chemical partitioned to 6 compartments (air, soil, water, suspended sediment, sediment, biota) within a unit world. Level I data are basic partitioning data that allow for comparisons between chemicals and indicate the compartment(s) to which a chemical is likely to partition.

The EQC Level I is a steady state, equilibrium model that utilizes the input of basic chemical properties including molecular weight, vapor pressure, and water solubility to calculate distribution within a standardized regional environment. This model will be used to calculate distribution values for representative chemical components identified in products in this category. A computer model, EPIWIN – version 3.02 (EPIWIN, 1999), will be used to calculate the properties needed to run the Level I EQC model. This information will be summarized in robust summaries for this group of products.

IV. TEST PLAN SUMMARY

ExxonMobil Chemical Company believes that the Neoacids C5-C28 Category of chemicals should be further examined in the following manner:

- Conduct Ames assays on Propanoic acid, 2,2-dimethyl- (CAS# 75-98-9) and 2,2-dimethyloctanoic acid (CAS# 26898-20-8) to evaluate the mutagenic potential of Neoacids C5-C28.
- Conduct mouse micronucleus assays Propanoic acid, 2,2-dimethyl- (CAS# 75-98-9) and 2,2-dimethyloctanoic acid (CAS# 26898-20-8) to evaluate the clastogenic potential of Neoacids C5-C28.
- Calculate physicochemical data as described in the EPA document titled, *The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program* for selected chemical components of the neo acid products in this category. Provide measured data for selected products where readily available.
- Prepare a technical discussion on the potential of neo acid products in this category to photodegrade. Calculate AOP values for selected chemical components of neoacid products in this category.
- Prepare a technical discussion on the potential of neo acid products in this category to hydrolyze. Calculate the hydrolysis rate of Propanoic acid, 2,2-dimethyl-, methyl ester (CAS# 598-98-1).
- Calculate fugacity data for selected chemical components of neo acid products in this category.
- Conduct a fish acute toxicity test with Fatty acids, C9-13 neo (CAS# 68938-07-8).

- Conduct a Daphnid acute toxicity test with Fatty acids, C9-13 neo (CAS# 68938-07-8).
- Conduct algal toxicity tests with Propanoic acid, 2-2-dimethyl- (CAS# 75-98-9) and 2,2-dimethyloctanoic acid (CAS# 26898-20-8).

ExxonMobil Chemical Company believes the thorough evaluation of the strategic anchor studies, the development of selected information and data, and the overall robustness of the final screening data set for the Neoacids C5-C28 Category complies with the objectives of the HPV volunteer testing program.

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**Table 3. Assessment Plan for the Neoacids C5-C28 Category Under the Program.
(Robust summaries for existing studies are submitted separately.)**

Stream Description	Human Health Effects						Ecotoxicity			Physical Chem. ¹	Environmental Fate			
	Acute Toxicity	Genetic Point Mut.	Genetic Chrom.	Sub-chronic	Developmental	Reproduction	Acute Fish	Acute Invert.	Algal Toxicity		Photo-deg.	Hydrolysis	Fugacity	Biodeg.
Propanoic acid, 2,2-dimethyl-	A	T	T	A	RA	RA	A	A	T	CM/M	CM	CM	CM	A
Propanoic acid, 2,2-dimethyl-, methyl ester	RA	RA	RA	RA	RA	RA	RA	RA	RA	CM/M	CM	CM	CM	RA
Carboxylic acid, C6-8 neo	A	RA	RA	A	A	A	A	A	A	CM/M	CM	CM	CM	A
2,2-Dimethyloctanoic acid	A	RA	RA	A	RA	A	A	A	RA	CM/M	CM	CM	CM	A
Fatty acids, C9-13 neo	RA	RA	RA	RA	RA	A	T	T	T	CM/M	CM	CM	CM	A
Fatty acids, C9-28 neo	RA	T	T	RA	RA	RA	RA	RA	RA	CM/M	CM	CM	CM	RA

¹ Measured data for selected physicochemical endpoints will be identified in conjunction with calculated data to characterize this category.

A Adequate existing data available

TD Technical Discussion proposed

RA Read Across (see Sec. III.B)

CM Computer Modeling proposed

T Testing proposed

M Measured data where available

NA Not Applicable

AR201-13335B

Neoacids C5-C28 Category

**Robust Summaries
(Environmental Fate and Effects)**

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Prepared by:

ExxonMobil Chemical Company

November 15th, 2001

Table of Contents

CAS # 75-98-9; C5 Neo Acid, Propanoic acid, 2,2-dimethyl-
Invertebrate Acute Toxicity
Fish Acute Toxicity
Biodegradation - Manometric Respirometer

CAS # 95823-36-2; C6-8 Neo Acid, Carboxylic acid
Biodegradation - Manometric Respirometry
Fish Acute Toxicity - Flow Through
Algal Toxicity

CAS # 26896-20-8; C10 Neo Acid, 2,2-Dimethyl-octanoic acid
Biodegradation -Manometric Respirometry
Invertebrate Acute Toxicity
Fish Acute Toxicity

CAS # 68938-07-8; C9-13 Neo Acid, Fatty Acids C9-13
Biodegradation -Manometric Respirometry

Robust Summaries - Neoacids C5-C28

Invertebrate Acute Toxicity

Test Substance:	Propanoic acid, 2,2-dimethyl (C5)																													
Method/Guideline:	USEPA -660/3-75-009 Methods for Acute Toxicity with Fish and Macroinvertebrates, and Amphibians, 1975																													
Type (test type):	Daphnid Acute Toxicity Test																													
GLP:	Unknown																													
Year (study performed):	1977																													
Species:	Water Flea (Daphnia magna)																													
Analytical Monitoring:	No																													
Exposure Period:	48 hour																													
Statistical Method:	Moving Average-Angle Method, (Harris 1959)																													
Test Conditions:	<p>For each test concentration, the appropriate amount of test substance was dissolved in ethanol and pipetted into 500ml of dilution water. This solution was mixed with a magnetic stirrer and divided into three 150ml replicates for testing. The remaining 50ml was used for pH and dissolved oxygen measurements. A positive control (with ethanol) and a negative control (dilution water) were also tested. Test vessels were 250ml beakers containing five daphnids each. Dilution water was reconstituted deionized water with a hardness of 180mg/L as CaCO3, with a pH of 8.0. The test was performed under static conditions with no aeration.</p> <p>Nominal test concentrations were 36, 60, 100, 170, 280, and 460 mg/L</p> <p>Test temperature was 22+/- 1 Deg C. Dissolved oxygen ranged from 8.6 to 8.8 mg/L during the study. The pH of the test solutions varied from Control - 8.3; 36 mg/L - 8.2; 170 mg/L - 7.6; and 460 mg/L - 5.2.</p> <p>Organisms were supplied by in-house cultures. Age = <24 hours old</p>																													
<ul style="list-style-type: none">Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, loading.																														
Results:	LC50 = 202.94 mg/L (95% CI 241.23 to 168.21) based upon nominal test concentrations.																													
Units/Value:																														
<ul style="list-style-type: none">Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.	<table><tr><th rowspan="2">Test Concentration</th><th colspan="2">Mean % Mortality</th></tr><tr><th>24 hr.</th><th>48 hr.</th></tr><tr><td>Positive Control</td><td>0</td><td>0</td></tr><tr><td>Negative Control</td><td>0</td><td>0</td></tr><tr><td>36 mg/L</td><td>0</td><td>0</td></tr><tr><td>60 mg/L</td><td>0</td><td>0</td></tr><tr><td>100 mg/L</td><td>0</td><td>7</td></tr><tr><td>170 mg/L</td><td>7</td><td>13</td></tr><tr><td>280 mg/L</td><td>20</td><td>93</td></tr><tr><td>460 mg/L</td><td>100</td><td>100</td></tr></table>	Test Concentration	Mean % Mortality		24 hr.	48 hr.	Positive Control	0	0	Negative Control	0	0	36 mg/L	0	0	60 mg/L	0	0	100 mg/L	0	7	170 mg/L	7	13	280 mg/L	20	93	460 mg/L	100	100
Test Concentration	Mean % Mortality																													
	24 hr.	48 hr.																												
Positive Control	0	0																												
Negative Control	0	0																												
36 mg/L	0	0																												
60 mg/L	0	0																												
100 mg/L	0	7																												
170 mg/L	7	13																												
280 mg/L	20	93																												
460 mg/L	100	100																												
Conclusion:	Test substance is considered to be of low toxicity																													
Reliability:	Code 2, Reliable with Restriction																													

Robust Summaries - Neoacids C5-C28

Lack of analytical verification, concentration of ethanol unknown, missing pH value of 280mg/L concentration, quality assurance unknown.

Reference:

EG&G Bionomics, Wareham, Mass.

Other (source):

ExxonMobil Biomedical Sciences, Inc.

Fish Acute Toxicity

Test Substance:	Propanoic acid, 2,2-dimethyl (C5)
Method/Guideline:	Standard Methods for the Examination of Water and Wastewater Method #231, 1971
Type (test type):	Fish Static Acute Toxicity Test
GLP:	No
Year (study performed):	1979
Species:	Gold Fish (<i>Crassius auratus</i>)
Analytical Monitoring:	Yes
Exposure Period:	96 hour
Statistical Method:	Interpolation of graph of log of concentration (APHA 1971)
Test Conditions:	<p>The test material was added to ~30 L glass tank containing laboratory dilution water. Each chemical was tested in a series of concentrations in 25 L of solution. All tanks contained 10 fish. All test solutions were aerated unless it was a volatile compound.</p> <p>Test temperature was 20 +/- 1 Deg C., Lighting was not reported Dissolved Oxygen = test solutions aerated during study. The pH was 5.4.</p> <p>Fish Mean Wt.= 3.3 +/- 1.0g. Mean Total length = 6.2 +/-cm, Test Loading = 1.3 g of fish/L.</p>
<ul style="list-style-type: none">Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.	
Results:	
Units/Value:	LC50 = 380mg/L
<ul style="list-style-type: none">Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.	Analytical method used was Total Organic Carbon or by extraction and subsequent GC analysis.
Conclusion:	Test substance is considered to have low toxicity
Reliability:	Code 2, Reliable with Restriction
	Minimal data presented (i.e. lacking conc. series, analytical measurements, Dissolved Oxygen measurements).
Reference:	Bridie, A.L. et al., The Acute Toxicity Test of some Petrochemicals to Goldfish. Water Research Vol. 13. 1979
Other (source):	ExxonMobil Biomedical Sciences, Inc.

Robust Summaries - Neoacids C5-C28

Biodegradation

Test Substance:	Propanoic acid 2,2-dimethyl (C5)												
Method/Guideline:	OECD 301F, 1992												
Type (test type):	Manometric Respirometry Test												
GLP:	Yes												
Year (study performed):	1996												
Inoculum:	Domestic activated sludge												
Exposure Period:	28 days												
Test Conditions:	<p>Non acclimated activated sludge and test medium were combined prior to test material addition. Test medium consisted of glass distilled water and mineral salts (Phosphate buffer, Ferric chloride, Magnesium sulfate, Calcium chloride). Test vessels were 1L glass flasks placed in a waterbath and electronically monitored for oxygen consumption. Test material was tested in triplicate, controls and blanks were tested in duplicate. Test material concentration was between 31 and 50 mg/L. Sodium benzoate (positive control) concentration was 44mg/L. Test temperature was 22 +/- 1 Deg C.</p> <p>All test vessels were stirred constantly for 28 days using magnetic stir bars and plates.</p>												
<ul style="list-style-type: none">Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, loading.													
Results:													
Units/Value:	<p>Test material was not readily biodegradable. Half-life was not reached. By day 28, 24% degradation of the test material was observed. 10% biodegradation was achieved on day 20. By day 14, >60% biodegradation of positive control was observed, which meets the guideline requirement. No excursions from the protocol were noted. Biodegradation was based on oxygen consumption and the theoretical oxygen demand of the test material as calculated using results of an elemental analysis of the test material.</p>												
<ul style="list-style-type: none">Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.													
	<table><tr><td></td><td>% Degradation* (day 28)</td><td>Mean % Degradation (day 28)</td></tr><tr><td>Sample</td><td></td><td></td></tr><tr><td>Test Material</td><td>18.9, 42.7, 10.7</td><td>24.1</td></tr><tr><td>Na Benzoate</td><td>98.9, 95.5</td><td>97.2</td></tr></table> <p>* replicate data</p>		% Degradation* (day 28)	Mean % Degradation (day 28)	Sample			Test Material	18.9, 42.7, 10.7	24.1	Na Benzoate	98.9, 95.5	97.2
	% Degradation* (day 28)	Mean % Degradation (day 28)											
Sample													
Test Material	18.9, 42.7, 10.7	24.1											
Na Benzoate	98.9, 95.5	97.2											
Conclusion:	Test substance is considered not readily biodegradable.												
Reliability:	Code 1, Reliable without Restrictions												
Reference:	Exxon Biomedical Sciences Inc., Ready Biodegradability : OECD 301F Manometric Respirometry Test. 136894A..												
Other (source):	ExxonMobil Biomedical Sciences, Inc.												

Robust Summaries - Neoacids C5-C28

Biodegradation

Test Substance: Carboxylic acid, C6-8 neo

Method/Guideline: OECD 301F, 1992

Type (test type): Manometric Respirometry Test

GLP: Yes

Year (study performed): 1996

Inoculum: Domestic activated sludge

Exposure Period: 28 days

Test Conditions:

- Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, loading.**

Non acclimated activated sludge and test medium were combined prior to test material addition. Test medium consisted of glass distilled water and mineral salts (Phosphate buffer, Ferric chloride, Magnesium sulfate, Calcium chloride).

Test vessels were 1L glass flasks placed in a waterbath and electronically monitored for oxygen consumption.

Test material was tested in triplicate, controls and blanks were tested in duplicate.

Test material concentration was between 31 and 50 mg/L. Sodium benzoate (positive control) concentration was 44mg/L.

Test temperature was 22 +/- 1 Deg C.

All test vessels were stirred constantly for 28 days using magnetic stir bars and plates.

Results:

Units/Value:

- Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**

Test material was not readily biodegradable. Half-life was not reached. By day 28, 44% degradation of the test material was observed. 10% biodegradation was achieved on day 19

By day 14, >60% biodegradation of positive control was observed, which met the guideline requirement. No excursions from the protocol were noted.

Biodegradation was based on oxygen consumption and the theoretical oxygen demand of the test material as calculated using results of an elemental analysis of the test material.

<u>Sample</u>	<u>% Degradation*</u> <u>(day 28)</u>	<u>Mean % Degradation</u> <u>(day 28)</u>
Test Material	62.8, 24.6, 44.6	44.0
Na Benzoate	98.9, 95.5	97.2

* replicate data

Conclusion: Test substance is considered not readily biodegradable.

Reliability: Code 1, Reliable without Restrictions

Reference: Exxon Biomedical Sciences Inc., Ready Biodegradability : OECD 301F Manometric Respirometry Test. 136894A..

Other (source): ExxonMobil Biomedical Sciences, Inc.

Fish Acute Toxicity

Test Substance:	Carboxylic acid, C6-8 neo
Method/Guideline:	US EPA TSCA 797.1400
Type (test type):	Fish Acute Flow-through Toxicity Test
GLP:	Yes
Year (study performed):	1993
Species:	Fathead Minnow (<i>Pimephales promelas</i>)
Analytical Monitoring:	Yes
Exposure Period:	96 hour
Statistical Method:	Graphical (EPA-600/4-90-027)
Test Conditions:	<p>A stock solution of 900mg/L was prepared daily and administered via a stainless steel and glass proportional diluter to achieve the desired study concentrations. The stock solution was mixed for 30 minutes and adjusted to a pH of 7.5 +/- 0.1 as needed. All test material went into solution. The test chambers were duplicate 1L glass dishes located within 19L glass aquaria with a flow rate of 6 dish volumes per day. Each dish contained 10 fish.</p> <p>Test temperature was 22.8 Deg C., Lighting was 16 hours light : 8 hours dark with 51.8 to 52.9 ft-candles during full daylight periods. Dissolved Oxygen at initiation ranged from 8.4 to 8.5 mg/L and from 6.6 to 8.0 mg/L at termination. The pH was ranged from 7.6 to 7.2 during the study.</p> <p>Fish Mean Wt.= 0.065g. Mean Total length = 1.6cm, Test Loading = 0.11 g of fish/L.</p>
<ul style="list-style-type: none"> Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading. 	

Results:

LC50 = 630mg/L, based upon measured concentrations.

Units/Value:

Analytical method used was GC-FID

- Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**

<u>Nominal Conc.</u>	<u>Measured Conc.</u>	<u>% Mortality @ 96 hr.</u>
Control	<0.79 mg/L	0
56.25 mg/L	51.4 mg/L	0
112.5 mg/L	124 mg/L	0
225 mg/L	200 mg/L	0
450 mg/L	436 mg/L	0
900 mg/L	882 mg/L	0

Robust Summaries - Neoacids C5-C28

Conclusion:	Test substance is considered low toxicity
Reliability:	Code 1, Reliable without Restrictions
Reference:	Exxon Biomedical Sciences, Inc. Fish Acute Flow-through Toxicity Test, 148641.
Other (source):	ExxonMobil Biomedical Sciences, Inc.

Robust Summaries - Neoacids C5-C28

Algal Toxicity

Test Substance: Carboxylic acid, C6-8 neo

Method/Guideline: US EPA TSCA 40 CFR792.1989

Type (test type): Algal Toxicity Test

GLP: Yes

Year (study performed): 1993

Species/Strain: Fresh water Green Algae (*Selenastrum capricornutum*)

Analytical Monitoring: Yes

Exposure Period: 72 hour

Statistical Method: Linear Interpolation

Test Conditions:

- Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organism culture, age.**

A 500mg/L stock solution was prepared by adding the appropriate amount of test substance to algal nutrient media in an aspirator bottle. The stock solution was mixed for 15 minutes at <10% vortex on a magnetic stir plate. After mixing the solution was drawn out the bottom port. The pH was adjusted to 7.5 +/- 0.1 as necessary. The stock was diluted with algal nutrient media to prepared test solutions. Three replicates and a media/toxicant blank were prepared for each concentration. Replicate vessels were 125ml autoclaved Erlenmeyer flasks sealed with gauze stoppers. Test flasks (except blanks) were inoculated with ~1.0E⁴ cells/ml of algae. All test vessels were placed on a shaker table at ~100 rpm during the study.

Nominal treatment levels were 8.0, 31.0, 62, 125, and 250mg/L

Test temperature was 23.9 Deg. C. Lighting was continuous at 399.8 to 411.65 ft candles. The pH was 7.5 at test initiation and ranged from 7.4 to 7.6 at test termination.

Results:

Units/Value:

96 hour EC50 = 6.49mg/L (95% CI 5.64 to 7.54) based upon initial measured values (day 0).

Measurement (cells/growth)

Analytical method used was Headspace Gas Chromatography with Flame Ionization Detection (GC-FID).

- Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**

<u>Nominal Conc.</u> (mg/L)	<u>Measured Conc.</u> Day 0 (mg/L)	<u>Mean Cells</u> at 96 hr	<u>% Inhibition</u> at 96 hr
Control	0	2.3 E6	-
3.12	3.03	2.3 E6	0
6.25	6.20	1.2 E6	47.8
12.5	12.24	4.8 E5	79.1
25.0	23.55	4.2 E5	81.7
50.0	52.15	3.6 E5	84.3

Conclusion:

Test substance is considered moderately toxic

Robust Summaries - Neoacids C5-C28

Reliability:	Code 1, Reliable without Restrictions
Reference:	Exxon Biomedical Sciences Inc., Algal Acute Toxicity Test, 148667
Other (source):	ExxonMobil Biomedical Sciences, Inc.

Robust Summaries - Neoacids C5-C28

Biodegradation

Test Substance: 2,2-Dimethyloctanoic Acid (C10)

Method/Guideline: OECD 301F, 1992

Type (test type): Manometric Respirometry Test

GLP: Yes

Year (study performed): 1996

Inoculum: Domestic activated sludge

Exposure Period: 28 days

Test Conditions:

- Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, loading.**

Non acclimated activated sludge and test medium were combined prior to test material addition. Test medium consisted of glass distilled water and mineral salts (Phosphate buffer, Ferric chloride, Magnesium sulfate, Calcium chloride).

Test vessels were 1L glass flasks placed in a waterbath and electronically monitored for oxygen consumption.

Test material was tested in triplicate, controls and blanks were tested in duplicate.

Test material concentration was between 31 and 50 mg/L. Sodium benzoate (positive control) concentration was 44mg/L.

Test temperature was 22 +/- 1 Deg C.

All test vessels were stirred constantly for 28 days using magnetic stir bars and plates.

Results:

Units/Value:

- Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**

Test material was not readily biodegradable. Half-life was not reached. By day 28, 11% degradation of the test material was observed. 10% biodegradation was achieved on day 27

By day 14, >60% biodegradation of positive control was observed, which met the guideline requirement. No excursions from the protocol were noted.

Biodegradation was based on oxygen consumption and the theoretical oxygen demand of the test material as calculated using results of an elemental analysis of the test material.

<u>Sample</u>	<u>% Degradation*</u> <u>(day 28)</u>	<u>Mean % Degradation</u> <u>(day 28)</u>
Test Material	20.5, 3.60, 8.90	11.0
Na Benzoate	98.9, 95.5	97.2

* replicate data

Conclusion: Test substance is considered not readily biodegradable.

Reliability: Code 1, Reliable without Restrictions

Reference: Exxon Biomedical Sciences Inc., Ready Biodegradability : OECD 301F Manometric Respirometry Test. 136894A..

Other (source): ExxonMobil Biomedical Sciences, Inc.

Robust Summaries - Neoacids C5-C28

Invertebrate Acute Toxicity

Test Substance:	2,2-Dimethyloctanoic Acid (C10)																																			
Method/Guideline:	USEPA -660/3-75-009 Methods for Acute Toxicity with Fish and Macroinvertebrates, and Amphibians, 1975																																			
Type (test type):	Daphnid Acute Toxicity Test																																			
GLP:	No																																			
Year (study performed):	1977																																			
Species:	Water Flea (Daphnia magna)																																			
Analytical Monitoring:	No																																			
Exposure Period:	48 hour																																			
Statistical Method:	Moving Average-Angle Method, (Harris 1959)																																			
Test Conditions:	<p>For each test concentration, the appropriate amount of test substance was dissolved in triethylene glycol (TEG) and pipetted into 500ml of dilution water. This solution was mixed with a magnetic stirrer and divided into three 150ml replicates for testing. The remaining 50ml was used for pH and dissolved oxygen measurements. A positive control (with TEG) and a negative control (dilution water) were also tested. Test vessels were 250ml beakers containing five daphnids each. Dilution water was reconstituted deionized well water with a hardness of 180mg/L as CaCO3, with a pH of 8.0. The test was performed under static conditions with no aeration.</p> <p>Nominal test concentrations were 13, 22, 36, 60, 100, 170, and 280 mg/L</p> <p>Test temperature was 22+/- 1 Deg C. Dissolved oxygen ranged from 8.6 to 8.8 mg/L during the study. The pH of the test solutions ranged from 7.1 to 8.2.</p> <p>Organisms were <24 hrs old, supplied by in-house cultures</p>																																			
• Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, loading.																																				
Results:	LL50 = 47.1 mg/L (95% CI 33.6 to 57.8) based upon nominal test concentrations.																																			
Units/Value:	<table><tr><td></td><td colspan="2">Mean % Mortality</td></tr><tr><td>Test Concentration</td><td>24 hr.</td><td>48 hr.</td></tr><tr><td>Positive Control</td><td>0</td><td>0</td></tr><tr><td>Negative Control</td><td>0</td><td>0</td></tr><tr><td>13 mg/L</td><td>0</td><td>13</td></tr><tr><td>22 mg/L</td><td>0</td><td>13</td></tr><tr><td>36 mg/L</td><td>0</td><td>20</td></tr><tr><td>60 mg/L</td><td>20</td><td>67</td></tr><tr><td>100 mg/L</td><td>53</td><td>100</td></tr><tr><td>170 mg/L</td><td>87</td><td>100</td></tr><tr><td>280 mg/L</td><td>73</td><td>100</td></tr></table>				Mean % Mortality		Test Concentration	24 hr.	48 hr.	Positive Control	0	0	Negative Control	0	0	13 mg/L	0	13	22 mg/L	0	13	36 mg/L	0	20	60 mg/L	20	67	100 mg/L	53	100	170 mg/L	87	100	280 mg/L	73	100
	Mean % Mortality																																			
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100 mg/L	53	100																																		
170 mg/L	87	100																																		
280 mg/L	73	100																																		
• Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.																																				
Conclusion:	Test substance is considered to be of moderate toxicity																																			

Robust Summaries - Neoacids C5-C28

Reliability:

Code 2, Reliable with Restrictions

Lack of measured concentrations, no documentation of pH adjustment of treatments.

Reference:

EG&G Bionomics, Wareham, Mass. BW-78-1-005

Other (source):

ExxonMobil Biomedical Sciences, Inc.

Fish Acute Toxicity

Test Substance:	2,2-Dimethyloctanoic Acid (C10)
Method/Guideline:	OECD 203 Fish Acute Toxicity Test
Type (test type):	Fish Acute Toxicity Test
GLP:	Yes
Year (study performed):	1996
Species:	Rainbow Trout (<i>Oncorhynchus mykiss</i>)
Analytical Monitoring:	Yes
Exposure Period:	96 hour
Statistical Method:	Bionomial Method
Test Conditions:	<p>Individual Water Accomodated Fractions (WAF's) were prepared for each test treatment. The test substance was added volumetrically, via a syringe, to 19L of dilution water in a 20L glass carboy. The solution was mixed for 24 hours at a vortex of $\leq 10\%$ of the total depth. After mixing the mixtures were adjust for pH to that of the dilution water using 1.0m NaOH. The test solutions were pumped from each mixing vessel into three replicates of 4.5L in 4.0L glass aspirator bottles (no headspace). Five fish were added to each test replicate and the replicates sealed. Daily renewals were performed by removing $\sim 80\%$ of the test solution through the port at the bottom and refilling with fresh solution.</p> <p>Test temperature was 15.0 Deg C., Lighting was 19 hours light : 5 hours dark with 528 to 538 Lux during full daylight periods. Dissolved Oxygen at initiation ranged from 8.5 to 9.0 mg/L and from 5.9 to 7.4 mg/L in "old" solutions prior to renewals. The pH was ranged from 7.0 to 7.6 during the study. Fish were not fed during the study.</p> <p>Fish Mean Wt. = 0.260g. Mean Total length = 3.3cm, Test Loading = 0.29 g of fish/L.</p>
Results:	LC50 = 37.2mg/L (CI 26.3 to 52.5), based upon measured concentrations of mean of old and new samples.
Units/Value:	<p>Analytical method used was GC-FID</p> <p>LL50 = 35.4 mg/L (CI 25.0 to 50.0), based upon nominal loading levels.</p>
<ul style="list-style-type: none"> Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading. 	
<ul style="list-style-type: none"> Note: Deviations from protocol or guideline, analytical method, biological observations, control survival. 	

Robust Summaries - Neoacids C5-C28

Results continued	<u>Nominal Conc.</u>	<u>Measured Conc.</u>	<u>% Mortality @ 96 hr.</u>
	Control	Below detection	0
	6.25 mg/L	10.3 mg/L	0
	12.5 mg/L	13.6 mg/L	0
	25 mg/L	26.3 mg/L	0
	50 mg/L	52.5 mg/L	100
	100 mg/L	102 mg/L	100
Conclusion:	Test substance is considered moderate toxicity		
Reliability:	Code 1, Reliable without Restrictions		
Reference:	Exxon Biomedical Sciences, Inc. Fish Acute Toxicity Test, 118358.		
Other (source):	ExxonMobil Biomedical Sciences, Inc.		

Robust Summaries - Neoacids C5-C28

Biodegradation

Test Substance: Fatty Acids C9-13, Neo 913 Acid

Method/Guideline: OECD 301F, 1992

Type (test type): Manometric Respirometry Test

GLP: Yes

Year (study performed): 1996

Inoculum: Domestic activated sludge

Exposure Period: 28 days

Test Conditions:

- Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, loading.**

Non acclimated activated sludge and test medium were combined prior to test material addition. Test medium consisted of glass distilled water and mineral salts (Phosphate buffer, Ferric chloride, Magnesium sulfate, Calcium chloride).

Test vessels were 1L glass flasks placed in a waterbath and electronically monitored for oxygen consumption.

Test material was tested in triplicate, controls and blanks were tested in duplicate.

Test material concentration was between 31 and 50 mg/L. Sodium benzoate (positive control) concentration was 44mg/L.

Test temperature was 22 +/- 1 Deg C.

All test vessels were stirred constantly for 28 days using magnetic stir bars and plates.

Results:

Units/Value:

- Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**

Test material was not readily biodegradable. Half-life was not reached. By day 28, 2.3% degradation of the test material was observed. 10% biodegradation was not achieved by day 28. By day 14, >60% biodegradation of positive control was observed, which met the guideline requirement. No excursions from the protocol were noted.

Biodegradation was based on oxygen consumption and the theoretical oxygen demand of the test material as calculated using results of an elemental analysis of the test material.

Sample	% Degradation* (day 28)	Mean % Degradation (day 28)
Test Material	4.50, 0.00, 2.50	2.33
Na Benzoate	98.9, 95.5	97.2

* replicate data

Conclusion: Test substance is considered not readily biodegradable.

Reliability: Code 1, Reliable without Restrictions

Reference: Exxon Biomedical Sciences Inc., Ready Biodegradability : OECD 301F Manometric Respirometry Test. 136894A..

Other (source): ExxonMobil Biomedical Sciences, Inc.

Robust Summaries - Neoacids C5-C28

Neoacids (C₅-C₂₈) Category

Robust Summaries (Mammalian Toxicity)

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Prepared by:

ExxonMobil Chemical Company

November 15, 2001

Table of Contents

CAS # 75-98-9; Propanoic acid, 2,2-dimethyl-

Acute Oral

Acute Dermal

Acute Inhalation

Repeat Dose - Dermal

CAS # 95823-36-2; Carboxylic acid, C6-8 neo

Acute Oral

Acute Dermal

Acute Inhalation

Repeat Dose - Dermal

Developmental Toxicity

CAS #26896-20-8; 2,2-Dimethyloctanoic acid

Acute Oral

Acute Dermal

Acute Inhalation (vapor)

Acute Inhalation (aerosol)

Repeat Dose - Dermal

Reproductive Toxicity

CAS # 25103-52-0; Isooctanoic acid (read-across)

Developmental Toxicity

Reproductive Toxicity

CAS #3302-10-1; Isononanoic acid (read-across)

Reproductive Toxicity

Robust Summaries - Neoacids C5-C28

Acute Toxicity

Test Substance CAS No.	Propanoic acid, 2,2-dimethyl- 75-98-9
Method/Guideline	Other
Type of Study	Acute oral toxicity
GLP	Pre-GLP
Year	1964
Species/strain	Sprague-Dawley Rats
Sex	Males
No. of animals/sex/dose	5/dose
Route of administration	Gastric Intubation
Vehicle	None
Frequency of Treatment	Single Dose
Dose/Concentration Levels	34.6, 120, 417, 1450, 5000, and 10000 mg/kg
Control group and Treatment	None
Remarks on Test Conditions	The animals were fasted for a period of three to four hours prior to treatment. The animals were observed for toxic effects and mortality at one, four and 24 hours; and once daily thereafter for 14 days. A necropsy was performed on any animal that died. All surviving animals were weighed, sacrificed and necropsied.
Results	LD ₅₀ = 2000 mg/kg Number of animals dead per number tested: 34.6, 120 and 417 mg/kg: 0/5 1450 mg/kg: 2/5 5000 mg/kg: 5/5 10,000 mg/kg: 5/5
Remarks	There were no deaths and no findings at necropsy in animals treated with 34.6, 120 and 417 mg/kg. At the 1450 mg/kg level, 2 of 5 animals died by day 2 and the remaining animals survived until the end of the study. These animals showed depression, severe dyspnea, depressed reflexes, sprawling, and lack of coordination. All animals in the 5000 and 10,000 mg/kg dose groups died within 48 hours of treatment. Severe depression, dyspnea, and prostration preceded death in all of the animals that died. Necropsy findings in high dose animals indicated congestion of lungs, liver, kidneys, and adrenals.
Conclusions	Under conditions of this study, Propanoic acid, 2,2-dimethyl- acid has a low order of acute oral toxicity in rats.
Data Quality	2 - Valid with restrictions (Pre-GLP)
Reference	Esso Research and Engineering Company (1964). Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report.
Date last changed	October, 2000

Robust Summaries - Neoacids C5-C28

Acute Toxicity

Test Substance CAS No.	Propanoic acid, 2,2-dimethyl- 75-98-9
Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Vehicle Frequency of Treatment Dose/Concentration Levels Control group and Treatment	Other Acute dermal toxicity Pre-GLP 1964 Rabbits/Albino Males and Females 2/sex/dose Dermal None Single Dose 50, 200, 794, 3160 mg/kg None
Remarks on Test Conditions	Undiluted test sample was applied to clipped, intact abdominal skin under a dental dam binder. The trunk was subsequently wrapped with gauze and adhesive tape. Following a 24-hour exposure period, binders were removed and the abdominal area was sponged with corn oil to remove sample residue. Following exposure, animals were observed for mortality or toxic effects at 1, 4, and 24 hours, and once daily thereafter for a total of 14 days. A necropsy was performed on any animal that died during the study. At the end of the 14-day observation period, all surviving animals were weighed, sacrificed, and necropsied.
Results	LD50 = 3160 mg/kg
Remarks	<p>In the highest dose group, two deaths occurred at 24 and 48 hours after exposure to the test substance. Death was preceded by marked depression, severe, dyspnea, prostration, excessive urination, and coma. Necropsy revealed congestion of the lungs, adrenals, kidneys, and blanched areas on the liver and spleen. In addition, inflammation of the bladder and gastrointestinal tract were noted. In the 794 mg/kg group, three of the four animals exhibited slight depression, dyspnea, unsteady gait with slight sprawling of the limbs at 24 hours after exposure to the test substance. However, by the third day post-exposure, all of the animals appeared normal. At the termination of the study, necrotic tissue was seen in the abdominal skin at the site of application of the test substance. Otherwise, no gross pathology was observed. In animals exposed to 50 and 200 mg/kg of the test substance, no signs of systemic toxicity were observed. These animals exhibited normal weight gain, appearance, and behavior.</p> <p>Dermal irritation was noted at all dose levels and was characterized by slight, transient erythema, edema, atonia, and desquamation at the lowest level. There was a dose-dependent increase in the intensity and persistence with pronounced irritation at the highest dose levels characterized by blanching, eschar formation, and necrosis.</p>
Conclusions	Under conditions of this study, Propanoic acid, 2,2-dimethyl- has a low order of acute dermal toxicity in rabbits.
Data Quality	2 - Valid with restrictions (Pre-GLP)
Reference	Esso Research and Engineering Company (1964). Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report.
Date last changed	January, 2001

Robust Summaries - Neoacids C5-C28

Acute Toxicity

Test Substance CAS No.	Propanoic acid, 2,2-dimethyl- 75-98-9
Method/Guideline	Other
Type of Study	Acute inhalation toxicity
GLP	Pre-GLP
Year	1964
Species/strain	Rats Wistar, Mice/Swiss albino
Sex	Males
No. of animals/sex/dose	10/species
Route of administration	Inhalation
Vehicle	Other
Frequency of Treatment	Single 6-hour exposure
Dose/Concentration Levels	Saturated vapors - the mean nominal concentration was 4.0 mg/L.
Control group and Treatment	A group of mice and rats that served as a common control for the substances tested in this study were sacrificed and examined grossly.
Remarks on Test Conditions	An atmosphere of saturated vapors was produced by forcing air through a bubbler system that contained the test substance. 29 ml of liquid was vaporized at a flow rate of 23 L/min. Animals were caged in wire mesh compartments within the exposure chamber. Animals were observed for mortality and toxic effects at 30-minute intervals during exposure and daily thereafter. The animals were observed for two weeks following exposure, at which point animals were sacrificed and necropsied. Any animals that died during the exposure or observation periods were necropsied.
Results	Mouse LC50 < 4.0 mg/L Rat > 4.0 mg/L
Remarks	No deaths occurred among any of the animals during the inhalation exposure. Hyperactivity followed by prostration was observed in mice. All 10 mice died within the 24 hours following exposure. Two rats died on the second and fifth days. Rats displayed piloerection, epistaxis, and dyspnea following exposure. Due to advanced autolysis, necropsy of the animals that died did not reveal any meaningful findings. Necropsy of the animals that survived until termination of the study did not reveal any significant gross pathology.
Conclusions	Propanoic acid, 2,2-dimethyl- has a moderate order of inhalation toxicity in rodents.
Data Quality	2 - Valid with restrictions - No vapor concentration verification (analytical)
Reference	Esso Research and Engineering Company (1964). Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report.
Date last changed	January, 2001

Robust Summaries - Neoacids C5-C28

Repeat Dose Toxicity

Test Substance	Propanoic acid, 2,2-dimethyl-
CAS No.	75-98-9
Method/Guideline	Other
Type of Study	Repeat dermal application
GLP	Pre-GLP
Year	1964
Species/strain	Albino Rabbits
Sex	Male
No. of animals/sex/dose	4/dose
Route of administration	Dermal
Vehicle	Isopropyl Alcohol (IPA)
Frequency of Treatment	10 applications with a two-day rest between the 5th and 6th applications.
Dose/Concentration Levels	30mg/kg and 300mg/kg weight/volume solution in isopropyl alcohol
Control group and Treatment	Isopropyl Alcohol (IPA) was administered to 8 animals at a level of 2.5 ml/kg body weight per application.
Statistical method	Not reported
Remarks on Test Conditions	<p>The test material was applied to clipped abdominal skin. A loose gauze binder or a collar was used to prevent ingestion of the test substance. Animals were housed individually and allowed free access to food and water. Each animal was weighed, sacrificed, and necropsied 24 hours after the final application of test material. At the beginning of the study and prior to the final application, the following clinical parameters were evaluated: total erythrocyte count, total and differential leukocyte count, hematocrit, and urinalysis. Histological analysis was performed on sections of liver and kidney. Sections of brain, thyroid, lungs, heart, liver, kidneys, adrenals, skin, and bone marrow were preserved for possible future analysis.</p>
Results	<p>For systemic effects: NOAEL = 300 mg/kg</p> <p>Propanoic acid, 2,2-dimethyl- produced moderate to severe skin irritation.</p>
Remarks	<p>The control animals exhibited normal appearance and behavior throughout the study with the exception of nasal discharge in one animal and diarrhea in another. Slight body weight loss was observed during the first week, but the animals regained the weight and most animals showed overall weight gains by the end of the study. No treatment-related effects were observed at gross necropsy. Repeat applications did not cause any histopathological alterations to the liver or kidney of the rabbits.</p> <p>Control animals exhibited slight erythema throughout the study and slight atonia and desquamation following the fifth application. Animals that received the test substance exhibited normal appearance and behavior throughout the study. Animals in the low dose group showed a net body weight gain by the end of the study and animals in the high dose group showed a slight weight loss by the end of the study. Gross pathological findings revealed parasitic infection of the liver and pitted kidneys in one rabbit, congested lungs in another, and congestion in the pancreas and kidney of a third rabbit. Slight to moderate erythema was observed in the low dose animals. Animals in the high dose group displayed moderate erythema, moderate edema, and moderate to marked atonia and desquamation. Three of the animals in the high dose group had areas of necrosis that persisted through the study.</p>

Robust Summaries - Neoacids C5-C28

Conclusions	Under the conditions of this study, Propanoic acid, 2,2-dimethyl- has a low order of systemic toxicity following repeated dermal exposure.
Data Quality	2 - Valid with restrictions (Pre-GLP)
Reference	Hazleton Laboratories, Inc. (1964) "Repeated Dermal Application - Rabbits," Unpublished report.
Date last changed	January 2001

Robust Summaries - Neoacids C5-C28

Acute Toxicity

Test Substance CAS No.	Carboxylic acid, C6-8 neo 95823-36-2
Method/Guideline	Other
Type of Study	Acute oral toxicity
GLP	Pre-GLP
Year	1964
Species/strain	Sprague-Dawley Rats
Sex	Males
No. of animals/sex/dose	5/dose
Route of administration	Gastric Intubation
Vehicle	None
Frequency of Treatment	Single Dose
Dose/Concentration Levels	34.6, 120, 417, 1450, 5000, and 10000 mg/kg
Control group and Treatment	None
Remarks on Test Conditions	The animals were fasted for a period of three to four hours prior to treatment. The animals were observed for toxic effects and mortality at one, four and 24 hours; and once daily thereafter for 14 days. Necropsy was performed on any animal that died. All surviving animals were weighed, sacrificed and necropsied.
Results	LD ₅₀ = 1860 mg/kg
Remarks	There were no principal toxic effects at 34.6, 120 and 417 mg/kg. In addition there were no findings at necropsy in these animals. At 1450 mg/kg, although there were no findings at necropsy, clinical signs were observed after dosing which included depression, dyspnea and slight to marked ataxia. At the two highest dose levels, all animals were dead within 24 hours. Prior to death, animals exhibited marked depression, sprawling of the limbs and depressed reflexes. Congestion of the lungs, kidneys and adrenals were observed in these animals.
Conclusions	Under conditions of this study, Carboxylic acid, C6-8 neo acid has a low order of acute oral toxicity in rats.
Data Quality	2 - Valid with restrictions (Pre-GLP)
Reference	Esso Research and Engineering Company (1964). Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report.
Date last changed	January, 2001

Robust Summaries - Neoacids C5-C28

Acute Toxicity

Test Substance CAS No.	Carboxylic acid, C6-8 neo 95823-36-2
Method/Guideline	Other
Type of Study	Acute dermal toxicity
GLP	Pre-GLP
Year	1964
Species/strain	Albino Rabbits
Sex	Males and Females
No. of animals/sex/dose	2/sex/dose
Route of administration	Dermal
Vehicle	None
Frequency of Treatment	Single Dose
Dose/Concentration Levels	50, 200, 794, 3160 mg/kg
Control group and Treatment	None
Remarks on Test Conditions	Undiluted test sample was applied to clipped, intact abdominal skin under a dental dam binder. The trunk was subsequently wrapped with gauze and adhesive tape. Following a 24-hour exposure period, binders were removed and the abdominal area was sponged with corn oil to remove sample residue. Following exposure, animals were observed for mortality or toxic effects at 1, 4, and 24 hours, and once daily thereafter for a total of 14 days. A necropsy was performed on any animal that died during the study. At the end of the 14-day observation period, all surviving animals were weighed, sacrificed, and necropsied.
Results	LD50 > 3160 mg/kg
Remarks	<p>One death occurred in the 200 mg/kg group at 48 hours post-exposure, but this was not considered to be treatment-related, since no deaths occurred in any of the other treatment groups. Upon necropsy, cecal obstruction and a large amount of fluid in the abdominal cavity were found. No signs of systemic toxicity were seen in any of the animals exposed to 50, 200, or 794 mg/kg. In the highest dose group, marked depression, dyspnea, ataxia, and sprawling of the limbs were observed 1 to 4 hours after application. However, the animals had completely recovered by 24 hours following exposure and exhibited normal appearance and behavior for the remainder of the 14-day post-exposure period. Necropsy revealed no significant signs of gross pathology in these animals.</p> <p>Dose-dependent dermal irritation occurred at all of the doses tested. This ranged from slight to moderate erythema, atonia, and desquamation at the lower dose levels to moderate erythema and edema with atonia and desquamation at the two higher dose levels.</p>
Conclusions	Under conditions of this study, Carboxylic acid, C6-8 neo acid has a low order of acute dermal toxicity in rabbits.
Data Quality	2 - Valid with restrictions (Pre-GLP)
Reference	Esso Research and Engineering Company (1964). Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report.
Date last changed	January, 2001

Robust Summaries - Neoacids C5-C28

Acute Toxicity

Test Substance	Carboxylic acid, C6-8 neo
CAS No.	95823-36-2
Method/Guideline	NA
Type of Study	Acute inhalation toxicity
GLP	Pre-GLP
Year	1964
Species/strain	Rats/Albino, Mice/Albino
Sex	Males
No. of animals/sex/dose	10/species
Route of administration	Inhalation
Vehicle	None
Frequency of Treatment	Single 6-hour exposure
Dose/Concentration Levels	Saturated vapors - the mean nominal concentration was 3.0 mg/L.
Control group and Treatment	Groups of mice and rats that served as common controls for the substances tested in this study were sacrificed and examined grossly.
Remarks on Test Conditions	An atmosphere of saturated vapors was produced by forcing air through a bubbler system that contained the test substance. 31 ml of liquid was vaporized at a flow rate of 27 L/min. Animals were caged in wire mesh compartments within the exposure chamber. Animals were observed for mortality and toxic effects at 30-minute intervals during exposure and daily thereafter. The animals were observed for two weeks following exposure, at which point animals were sacrificed and necropsied. Any animals that died during the exposure or observation periods were necropsied.
Results	LD50 > 3.0 mg/L
Remarks	No significant toxic signs were observed during the 6-hour exposure period. All mice and rats appeared normal up to 5 days following exposure, when the mice developed urticaria. No deaths occurred in mice or rats throughout the study and no significant observations were made at necropsy.
Conclusions	Under conditions of this study, Carboxylic acid, C6-8 neo has a low order of acute inhalation toxicity in mice and rats.
Data Quality	2 - Valid with restrictions - No vapor concentration verification (analytical)
Reference	Esso Research and Engineering Company (1964). Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report.
Date last changed	January, 2001

Robust Summaries - Neoacids C5-C28

Repeat Dose Toxicity

Test Substance	Carboxylic acid, C6-8 neo
CAS No.	95823-36-2
Method/Guideline	Other
Type of Study	Repeat dermal application
GLP	Pre-GLP
Year	1964
Species/strain	Albino Rabbits
Sex	Male
No. of animals/sex/dose	4/dose
Route of administration	Dermal
Vehicle	None
Frequency of Treatment	10 applications with a two-day rest between the 5th and 6th applications.
Dose/Concentration Levels	55.4 mg/kg, 553.7 mg/kg
Control group and Treatment	Isopropyl Alcohol (IPA) was administered to 8 animals at a level of 2.5 ml/kg body weight per application.
Statistical method	Not reported
Remarks on Test Conditions	<p>The test material was applied to clipped abdominal skin. A loose gauze binder or a collar was used to prevent ingestion of the test substance. Animals were housed individually and allowed free access to food and water. Each animal was weighed, sacrificed, and necropsied 24 hours after the final application of test material. At the beginning of the study and prior to the final application, the following clinical parameters were evaluated: total erythrocyte count, total and differential leukocyte count, hematocrit, and urinalysis. Histological analysis was performed on sections of liver and kidney. Sections of brain, thyroid, lungs, heart, liver, kidneys, adrenals, skin, and bone marrow were preserved for possible future analysis.</p>
Results	<p>For systemic effects: NOAEL = 553.7 mg/kg Carboxylic acid, C6-8 neo produced moderate to severe skin irritation.</p>
Remarks	<p>Animals in the low dose group showed normal appearance behavior throughout the study. With the exception of one animal that showed a slight weight loss, the animals in the low dose group showed an overall body weight gain. In the high dose group, 3 of the 4 animals displayed normal appearance and behavior and either maintained their weight or had a slight weight loss. From the fifth through the ninth application, the fourth animal had labored breathing, weight loss, and was found dead 24 hours after the final application. Upon necropsy, this animal had congested and emphysematous lungs in addition to hemorrhagic areas in the renal medulla. The death of this animal was deemed to be unrelated to the treatment. Gross pathology of the remaining animals of the high dose group did not reveal any abnormalities other than a slight parasitic infection in the liver of one of the rabbits. Repeat applications did not cause any histopathological alterations to the liver or kidney of the rabbits.</p> <p>In the low dose animals, slight erythema was observed during the first week, with slight to moderate atonia and desquamation that followed the third application and lasted through the study. At the highest dose, slight to moderate erythema was observed and slight to moderate edema was present from the second through the fifth applications. After the fourth application, moderate to marked atonia, desquamation, and slight fissuring was observed through the remainder of the study. All animals showed areas of necrosis at the application site and in two animals, the skin was hypersensitive to touch.</p>

Robust Summaries - Neoacids C5-C28

Conclusions	Under the conditions of this study, Carboxylic acid, C6-8 neo has a low order or systemic toxicity following repeated dermal exposure.
Data Quality	2 - Valid with restrictions (Pre-GLP)
Reference	Hazleton Laboratories, Inc. (1964) "Repeated Dermal Application - Rabbits," Unpublished report.
Date last changed	January 2001

Robust Summaries - Neoacids C5-C28

Developmental Toxicity

Test Substance CAS No.	Carboxylic acid, C6-8 neo 95823-36-2
Method	OECD 414
Type of Study	Developmental toxicity
GLP	Yes
Year	1986
Species/Strain	Sprague-Dawley Rats
Sex	Pregnant Females
Number/sex/dose	22/dose
Route of administration	Oral gavage
Exposure Period	Days 6-15 of gestation
Concentrations	0, 50, 250, 600, or 800 mg/kg
Controls	Controls received 800 mg/kg of distilled water
Statistical methods	ANOVA, Kruskal-Wallis, Fisher's exact test
Remarks on Test Conditions	<p>Physical examinations were performed and body weight and food consumption were measured throughout gestation. Mated females were sacrificed on gestational day 20 and a gross necropsy was performed. Uteri and ovaries were weighed and corpora lutea were counted. The number of implantation sites, early and late resorptions, and live and dead fetuses were determined. Full term fetuses were examined for abnormalities, weight, and crown-rump distance. From each litter, the heads of half of the fetuses were preserved and examined, while the other half of the fetuses were examined for skeletal malformations and ossification variations.</p>
<u>Results</u>	<p>NOAEL fetal: 250 mg/kg NOAEL maternal: 250 mg/kg</p>
Remarks for Results	<p>Maternal: The high dose of 800 mg/kg produced morbidity and mortality in 4 of the 22 mated females. This group displayed lethargy, abnormal breathing, rales, and staining around the muzzle and anogenital areas. Animals in the 600 mg/kg group had a significant incidence of rales. In the high dose group (800 mg/kg), maternal body weight gain and uterine weight at term were significantly reduced. In the 600 mg/kg group, there was a significant reduction in body weight gain during the intervals of gd6-9 and gd0-20. Maternal food consumption was significantly reduced during gestational intervals gd6-9 and gd9-12 for both the 600 and 800 mg/kg groups and during gd12-16 in the 800 mg/kg group.</p> <p>Fetus: In the high dose group, there was a significant increase in early embryonic resorptions with a corresponding decrease in the mean number of live fetuses. The remaining fetuses in the high dose group had significantly reduced fetal body weight and crown-rump distance. Microphthalmia and anophthalmia were observed in 14% of the fetuses from the high dose group. In addition, fused cervical vertebrae and misaligned thoracic vertebra were observed in the high dose group. Significant incidences of hydrocephalus and structural malformation of thoracic ribs occurred in both the 600 and 800 mg/kg groups. The fraction of malformed fetuses/live fetuses was significantly increased in the 600 and 800 mg/kg groups. In the 250 mg/kg group, there was an increase in the fraction of implants affected, however, this was not significantly different from the control group.</p>

Robust Summaries - Neoacids C5-C28

Results, continued	Visceral examination revealed that the incidence of renal/ureter variations was significantly increased in the high dose group. In addition, the high dose group showed an increased incidence of unossified structures of the cranium, sternum, vertebrae, pelvis, and hindpaw. In both the 600 and 800 mg/kg groups, there were increases in the incidences of incompletely ossified supraoccipital and cervical vertebrae.
Conclusions	Carboxylic acid, C6-8 neo is embryo-lethal and teratogenic in rats at doses that are maternally toxic. Under the conditions of this study, Carboxylic acid, C6-8 neo is not a selective developmental toxicant.
Data Quality	1 - Reliable without restrictions
Reference	Exxon Biomedical Sciences (1986) "Oral teratology study in rats," Unpublished study.
Date last changed	January, 2001

Robust Summaries - Neoacids C5-C28

Acute Toxicity

Test Substance	2,2-Dimethyloctanoic acid
CAS No.	26896-20-8
Method/Guideline	Other
Type of Study	Acute oral toxicity
GLP	Pre-GLP
Year	1964
Species/strain	Rats/Sprague-Dawley
Sex	Males
No. of animals/sex/dose	5/dose
Route of administration	Gastric Intubation
Vehicle	None
Frequency of Treatment	Single Dose
Dose/Concentration Levels	34.6, 120, 417, 1450, 5000, and 10000 mg/kg
Control group and Treatment	None
Remarks on Test Conditions	<p>The animals were fasted for a period of three to four hours prior to treatment. The animals were observed for toxic effects and mortality at one, four and 24 hours; and once daily thereafter for 14 days. Necropsy was performed on any animal that died. All surviving animals were weighed, sacrificed and necropsied.</p> <p>LD50= 2000 mg/kg</p>
Results	
Remarks	<p>There were no principal toxic effects or necropsy findings for animals in the 34.6, 120 and 417 mg/kg treatment groups. At 1450 mg/kg, 1 animal died within 24 hours of exposure and one animal died each day thereafter until all 5 animals were dead by day 5 of the study. Prior to death, slight to marked CNS depression, dyspnea, and ataxia was observed. In addition, congestion of the lungs, kidneys and adrenals were observed at necropsy. In the 5,000 mg/kg dose group, 2/5 animals died by 4 hours and 5/5 animals were dead by 24 hours following exposure. In the highest dose group, 4/5 animals died by 4 hours and all animals were dead by 24 hours post-treatment. Animals in the 5,000 and 10,000 mg/kg groups appeared to have depression, dyspnea, ataxia and sprawling of the limbs. Also at these two dose levels, necropsy findings indicated congestion of the lungs, liver, spleen, kidneys and adrenals.</p>
Conclusions	2,2-Dimethyloctanoic acid has a low order of acute oral toxicity in rodents.
Data Quality	2 - Valid with restrictions (Pre-GLP)
Reference	Esso Research and Engineering Company (1964). Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report.
Date last changed	October, 2000

Robust Summaries - Neoacids C5-C28

Acute Toxicity

Test Substance	2,2-Dimethyloctanoic acid
CAS No.	26896-20-8
Method/Guideline	NA
Type of Study	Acute dermal toxicity
GLP	Pre-GLP
Year	1964
Species/strain	Albino Rabbits
Sex	Males and Females
No. of animals/sex/dose	4/dose
Route of administration	Dermal
Vehicle	None
Frequency of Treatment	Single Dose
Dose/Concentration Levels	50, 200, 794, 3160 mg/kg
Control group and Treatment	None
Remarks on Test Conditions	<p>Undiluted test sample was applied to clipped, intact abdominal skin under a dental dam binder. The trunk was subsequently wrapped with gauze and adhesive tape. Following a 24-hour exposure period, binders were removed and the abdominal area was sponged with corn oil to remove sample residue. Following exposure, animals were observed for mortality or toxic effects at 1, 4, and 24 hours, and once daily thereafter for a total of 14 days. A necropsy was performed on any animal that died during the study. At the end of the 14-day observation period, all surviving animals were weighed, sacrificed, and necropsied.</p>
Results	LD50 > 3160 mg/kg
Remarks	<p>No deaths occurred with any of the doses tested. The animals appeared normal in appearance and behavior throughout the study. All of the animals exhibited a normal pattern of weight gain. No signs of gross pathology were observed at necropsy.</p> <p>No dermal irritation was observed at the 50 mg/kg dose level and minimal irritation characterized by slight erythema, atonia, and desquamation that subsided in 10 days was noted at the 200 mg/kg level. At the 794 and 3160 mg/kg levels, a dose-dependent increase in the degree of irritation was observed. This consisted of slight to moderate erythema, which subsided after the fourth and eighth days, and slight to moderate atonia and desquamation that diminished in severity through the 14-day period.</p>
Conclusions	Under conditions of this study, 2,2-Dimethyloctanoic acid has a low order of acute dermal toxicity in rabbits.
Data Quality	2 - Valid with restrictions (Pre-GLP)
Reference	Esso Research and Engineering Company (1964). Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report.
Date last changed	January, 2001

Robust Summaries - Neoacids C5-C28

Acute Toxicity

Test Substance	2,2-Dimethyloctanoic acid
CAS No.	26896-20-8
Method/Guideline	Other
Type of Study	Acute inhalation toxicity
GLP	Pre-GLP
Year	1964
Species/strain	Rats/Wistar, Mice/Swiss albino
Sex	Males
No. of animals/sex/dose	10/species
Route of administration	Inhalation
Vehicle	None
Frequency of Treatment:	Single 6-hour exposure
Dose/Concentration Levels:	Saturated vapors - the mean nominal concentration was 3.0 mg/L.
Control group and Treatment:	A group of mice and rats that served as a common control for the substances tested in this study were sacrificed and examined grossly.
Remarks on Test Conditions	An atmosphere of saturated vapors was produced by forcing air through a bubbler system that contained the test substance. 20 ml of liquid was vaporized at a flow rate of 21 L/min. Animals were caged in wire mesh compartments within the exposure chamber. Animals were observed for mortality and toxic effects at 30-minute intervals during exposure and daily thereafter. The animals were observed for two weeks following exposure, at which point animals were sacrificed and necropsied. Any animals that died during the exposure or observation periods were also necropsied.
Results	LD50 > 3.0 mg/L
Remarks	No mortality or significant signs of toxicity were observed during the 6-hour exposure period. No deaths occurred in mice or rats throughout the study and no significant observations were made at necropsy.
Conclusions	Under conditions of this study, 2,2-Dimethyloctanoic acid has a low order of acute inhalation toxicity in mice and rats.
Data Quality	2 - Valid with restrictions - No vapor concentration verification (analytical)
Reference	Esso Research and Engineering Company (1964). Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report.
Date last changed	January, 2001

Robust Summaries - Neoacids C5-C28

Acute Toxicity

Test Substance	2,2-Dimethyloctanoic acid
CAS No.	26896-20-8
Method/Guideline	Other
Type of Study	Acute inhalation toxicity
GLP	No
Year	1982
Species/strain	Rats/Wistar, Mice/Swiss albino, Guinea Pigs/Harley
Sex	Males and Females
No. of animals/sex/dose	10/sex/species
Route of administration	Inhalation
Vehicle	None
Frequency of Treatment	Single 6-hour exposure
Dose/Concentration Levels	Liquid aerosol with a mean analytical concentration of 511 mg/m ³
Control group and Treatment	10/sex/species
Remarks on Test Conditions	<p>Groups of animals (10/sex/species) were exposed to either air only or to aerosolized test material. Aerosol was generated by pumping the test material into an atomizer at 15.0 psi. The resulting aerosol was sprayed into a glass aerosol diffuser, where it was mixed with incoming room air before entering the chamber. Exposure concentrations were determined on both a nominal and actual (gravimetric) basis. Particle size determinations were conducted twice during exposure. During the exposure, control and treated animals were observed every 15 minutes for the first hour and hourly thereafter. On the first day post-exposure, one half of the animals from each group were randomly selected and sacrificed, and an interim necropsy was performed. The remaining animals were observed daily for signs of toxicity for 14 days post-exposure. Body weights were recorded at the beginning of the study, and at 1, 2, 3, 4, 7, and 14 days post-exposure. A necropsy was performed on all animals that died or were sacrificed during the study. Major organs were examined for macroscopic abnormalities and lungs plus trachea, liver, kidneys, whole head, and any abnormal tissues were preserved. Organ weights were recorded at necropsy for lungs plus trachea, liver, and kidneys.</p>
Results	LD50 > 511 mg/m ³
Remarks	<p>No animals died during the study. The control animals appeared normal throughout the exposure. During the two-week post-exposure period, incidences of ungroomed appearance, soft stool, and anogenital staining were observed in some of the control animals. One female guinea pig in the control group died on the fifth day of the post-exposure observation period.</p> <p>Animals exposed to the test material exhibited some signs of labored breathing, salivation, and eye irritation during the exposure. Upon removal from the chamber, exposed mice and guinea pigs had material-covered fur and exposed rats had some red staining around the nasal area, anogenital staining, soft stool, salivation, and lacrimation. During the two-week post-exposure observation period, all guinea pigs appeared normal. However, some of the mice appeared ungroomed and some rats exhibited anogenital staining and soft stool. Throughout the study, body weights remained normal except for a slight weight loss on the first and second post-exposure days in both the control and treated groups (all species).</p>

Robust Summaries - Neoacids C5-C28

Results, continued	At terminal sacrifice, male mice exposed to the aerosolized test substance exhibited a statistically significant decrease in the liver to body weight ratio versus control animals. No other statistically significant differences were observed for group mean organ weight to body weight ratios. Minor macroscopic abnormalities were observed in both control and treated groups at the interim and terminal necropsies, but were not considered to be related to exposure to the test substance.
Conclusions	Under conditions of this study, aerosolized 2,2-Dimethyloctanoic acid has a low order of acute inhalation toxicity in mice, rats, and guinea pigs.
Data Quality	1 - Valid without restrictions
Reference	Bio/dynamics, Inc. (1982) "Evaluation of the Acute inhalation Toxicity in Rats, Mice, and Guinea Pigs". Unpublished report.
Date last changed	January, 2001

Repeat Dose Toxicity

Test Substance CAS No.	2,2-Dimethyloctanoic acid 26896-20-8
Method Type of Study GLP Year Species/Strain	Other Repeat dermal application Pre-GLP 1964 Albino Rabbits
Sex Number/sex/dose Route of administration Vehicle Exposure Period Concentrations Controls	Male 4/dose Dermal None 10 applications with a two-day rest between the 5th and 6th applications. 0.4 g/kg and 2.28 g/kg Isopropyl Alcohol (IPA) was administered to 8 animals at a level of 2.5 ml/kg body weight per application.
Statistical method	Not reported
Remarks on Test Conditions	The test material was applied to clipped abdominal skin. A loose gauze binder or a collar was used to prevent ingestion of the test substance. Animals were housed individually and allowed free access to food and water. Each animal was weighed, sacrificed, and necropsied 24 hours after the final application of test material. At the beginning of the study and prior to the final application, the following clinical parameters were evaluated: total erythrocyte count, total and differential leukocyte count, hematocrit, and urinalysis. Histological analysis was performed on sections of liver and kidney. Sections of brain, thyroid, lungs, heart, liver, kidneys, adrenals, skin, and bone marrow were preserved for possible future analysis.
<u>Results</u>	For systemic effects: NOAEL = 2.28 g/kg 2,2-Dimethyloctanoic acid produced moderate skin irritation.
Remarks for Results	<p>Wheezing was noted in one animal of the low dose group. However, the rest of the animals appeared normal in behavior and appearance throughout the study. Animals in the low dose group showed overall body weight gain while animals in the high dose group had a slight reduction in weight at the end of the study. Necropsy revealed parasitic areas on the liver and/or mesentery of three animals, emphysema in three animals, and fluid in the cranial cavity and sinuses of one animal. These findings, however, did not correlate with the dose of test material received and were not attributed to exposure to the test substance. Animals in both the low and high dose groups displayed a decrease in terminal total leukocyte count. However, these values were within the normal limit value for rabbits. Repeat applications did not cause any histopathological alterations to the liver or kidney of the rabbits.</p> <p>Animals in the low dose group displayed slight erythema and moderate atonia and desquamation starting on the first or fourth application and persisting through the remainder of the study. All animals in the high dose group had moderate erythema, moderate to marked atonia and desquamation, and slight edema after the fifth application. After seven applications, slight fissures were observed in some of the animals and the exposed skin became hypersensitive to touch.</p>

Robust Summaries - Neoacids C5-C28

Conclusions	Under the conditions of this study, 2,2-Dimethyloctanoic acid has a low order of systemic toxicity following subchronic dermal exposure.
Data Quality	2 - Valid with restrictions (Pre-GLP)
Reference	Hazleton Laboratories, Inc. (1964) "Repeated Dermal Application - Rabbits," Unpublished report.
Date last changed	January 2001

Reproductive Toxicity

Test Substance	2,2-Dimethyloctanoic acid
CAS No.	26896-20-8
Method/Guideline	Other
Type of Study	Reproductive Toxicity
GLP	Pre-GLP
Year	1968
Species/strain	Rats/Sprague-Dawley
Sex	Males and Females
No. of animals/sex/dose	P ₁ : 80 females and 40 males
Route of administration	Dietary
Frequency of Treatment	Continuous
Dose/Concentration Levels	0, 100, 500, 1500 ppm in diet
Control group and Treatment	Purina Lab Chow, 0 ppm of test substance
Duration of Test	3 generations
Pre-mating Exposure Period	P ₁ : 9 weeks for both males and females
Remarks on Test Conditions	<p>Pre-mating Period: For each dose level, 10 males and 20 females comprised the P₁ generation. The parental generation animals were maintained in individual cages and fed the corresponding diet for 9 weeks prior to mating. Individual body weights, food consumption, and observations of the physical appearance and behavior of the animals were recorded initially, at 5 weeks, and 9 weeks (P₁), or at 8 weeks, and 12 weeks (P₂). The F2B weanlings (P₃) were fed the appropriate diets for 9 weeks and the same observations were recorded at 0, 8, and 9 weeks of exposure.</p> <p>Reproduction Period: Following 9 weeks of exposure, two females and 1 male from each group were housed together and allowed a 3-week mating period, during which time, males were rotated among the females on a weekly basis. 24 hours following birth of the F1A generation, litters were arbitrarily reduced to a maximum of 8 pups (4/sex) to be nursed. The number of conceptions, litters, live births, stillbirths, the size of natural and nursing litters, deaths during the period of lactation, and number of pups weaned were all recorded. The weights of the pups by sex were recorded at 24 hours and at weaning and all pups were observed for gross signs of abnormalities. Following the 21-day nursing period, representative pups from each litter were sacrificed and gross necropsies were performed. The remaining pups were discarded.</p> <p>One week following the weaning of the F1A litters, the P1 parents were re-mated in the same fashion to produce the F1B pups. Following the 21-day nursing period, 20 female and 10 male weanlings from each of the test groups were randomly designated as the P2 generation. The remaining F1B pups were sacrificed and necropsied. The P2 generation was fed the appropriate diet until 100 days of age and then mated in the same fashion to produce the F2A and F2B litters. The same procedures were followed as during the first reproductive phase. After the second litter, F2B, 20 females and 10 males were selected at random to be the P3 generation. Following 9 weeks of dietary administration to this generation, the study was terminated and gross necropsies were performed. The following tissues were preserved: brain, pituitary, eye, thyroid, lung, heart, liver, spleen, kidney, adrenal, stomach, pancreas, small and large intestine, urinary bladder, gonad, bone, bone marrow, and trachea. Tissues from 5 females and 5 males of the control and high dose groups underwent histological examination. In addition, sections of thyroid, lung, liver, kidney, adrenal and trachea from 5 females and 5 males of the low level and intermediate level groups were examined microscopically.</p>

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Results	NOAEL Parental: 1500 ppm NOAEL F1 Offspring: 1500 ppm NOAEL F2 Offspring: 1500 ppm
Remarks	<p>For all of the concentrations tested, no adverse effects were observed on survival, appearance, behavior, body weight gain, and food consumption in either the parental generation or either the F1 or F2 generations. In addition, the reproductive performance of the parents was not affected. No treatment-related gross or microscopic pathological findings were observed at any of the dietary levels.</p> <p>All of the P1 and P2 animals survived the pre-mating periods and all of the P3 animals survived the 9-week post-weaning period of exposure. The body weight gain, food consumption, appearance, and behavior of the rats in these test groups were comparable with that of the control rats. In the F1A and F1B litters, litter size, pup body weights, appearance, and behavior were comparable between the treated groups and the control group. There were a variety of incidental findings in pups of the F1A and F1B litters, however, pups of these litters did not display any signs of treatment-related toxicity. At necropsy, there were no gross alterations that could be attributed to exposure to the test substance. The F2A and F2B litters, similar to the F1 litters had incidental findings, but did not show any treatment-related signs of toxicity, or effects on litter size, pup body weights, appearance, or behavior. Examination of the F2B weanling pups also (P3) did not reveal any treatment-related abnormalities.</p>
Conclusions	Under the conditions of this study, dietary exposure to 2,2-Dimethyloctanoic acid has a low order of reproductive toxicity in rats.
Data Quality	2 - Valid with restrictions (Pre-GLP)
Reference	Hazleton Labs, Inc. (1968) "Modified Three-Generation Reproduction Study - Rats," Unpublished report.
Date last changed	January 2001

Robust Summaries - Neoacids C5-C28

Developmental Toxicity

<p>Test Substance CAS No.</p> <p>Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Vehicle: Dose/Concentration Levels Control group and Treatment Statistical methods</p> <p>Remarks on Test Conditions</p> <p>Results</p> <p>Remarks</p>	<p>Isooctanoic Acid 25103-52-0</p> <p>Other Developmental Toxicity Yes 1995 Rat/Sprague-Dawley Female 25/dose Oral gavage Corn oil 0, 50, 200, 400, 800, and 1000 mg/kg/day Vehicle control: corn oil Statistical evaluation of equality of means was done by appropriate one way analysis of variance. Also, a standard regression analysis for linear response in the dose groups was performed.</p> <p>Males and females were housed together until confirmation of mating. The presence of a sperm plug was set as gestational day (GD) 0. Mated females were dosed once daily from GD 6-15. Dosing volumes were 5 ml/kg for all groups and were based on the most recent body weight. Clinical observations were made daily during gestation. Food consumption and body weight measurements were made on every three days through GD21. On GD21, animals were euthanized and cesarean sections were performed. Gross necropsies were performed, uterine weights with ovaries were measured, uterine contents were examined, and uterine implantation data were recorded. All live fetuses were weighed, examined externally to determine sex and for gross malformations.</p> <p>Maternal NOAEL = 400 mg/kg/day Fetal NOAEL = 800 mg/kg/day</p> <p>Maternal: There were no treatment-related deaths during the study. However, there were some deaths in the different dose groups that were attributed to intubation errors. Animals in the 800 and 1000 mg/kg/day groups displayed clinical signs that included rales, stool abnormalities, and anogenital/abdominal staining following dose initiation on GD6. Animals in the remaining dose groups were free of clinical signs for the entire gestation period. Overall, there were no statistically significant differences in mean body weight gain for the entire gestation interval or the entire gestation interval corrected for uterine weight between treated and control animals. However, in the 800 and 1000 mg/kg/day groups, there were statistically significant decreases in body weight gain early during gestation (GD 6-15). This correlated with decreased mean food consumption in these groups during this time frame. In the 400 mg/kg/day group, there was evidence of slight body weight gain suppression during the interval following dosing. However, these animals recovered quickly and in the absence of a consistent response, this finding was considered the result of slight dosing trauma. There were no significant findings at necropsy other than some trauma that was indicative of dosing errors.</p>
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Results, continued	<p>Fetal: There were no statistically significant differences in reproductive parameters including: total live fetuses, sex ratio, mean number of resorptions, mean number of implantation sites, mean number of corpora lutea, mean fetuses per implantation site, mean resorptions per implantation site, % pre-implantation losses, % post-implantation loss, or mean total affected (resorptions + dead + malformed fetuses per litter) between treated and control animals. No external abnormalities were observed in any fetuses from the control or treated groups. In the highest dose group, a statistically significant decrease in mean male and female fetal body weights was observed compared with the controls.</p>
Conclusions	<p>Under the conditions of this study, Isooctanoic acid is not a selective developmental toxicant.</p>
Data Quality	<p>2- reliable with restrictions - range-finding study.</p>
Reference	<p>Exxon Biomedical Sciences, Inc. (1995). "Developmental toxicity range-finding study in rats," Unpublished report.</p>
Date last changed	<p>October 22, 2001</p>

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Reproductive Toxicity

<p>Test Substance CAS No.</p> <p>Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Dose/Concentration Levels Control group and Treatment Statistics</p>	<p>Isooctanoic Acid 25103-52-0</p> <p>Other One-Generation Reproductive Toxicity Yes 1999 Rat/Sprague-Dawley Males and Females 10/sex/dose Dietary 0, 1000, 5000, 7500, and 10,000 ppm in diet 10/sex For the statistical analysis the percent of normal sperm were transformed by Bloom's transformation. All variables were analyzed by standard one-way analysis of variance (ANOVA). Residuals from the model were tested for normality by the Shapiro-Wilk. When there were differences in-group means based on the ANOVA, differences in means were tested using Duncan's multiple range test.</p>
<p>Remarks on Test Conditions</p>	<p>P1 males and females (10 animals/sex) were exposed to the test substance for 10 weeks prior to mating. One male and one female were paired for up to 2 weeks. Beginning on GD 21, mated females were examined at least twice daily for signs of parturition. On PND 0, 1, 4, 7, 14 and 21 the offspring were counted, sexed and each live pup was weighed. Pups were counted and examined externally on a daily basis during the postnatal period. All animals were weighed and examined on PND 28, 35, 42, and 49 (males only were weighed and examined on PND Day 49). On PND 4, after counting, weighing, and examining the pups, the size of each litter was adjusted by eliminating extra pups by random selection to yield as nearly as possible, 4 males and 4 females per liter. Pups from each litter were examined daily for developmental landmarks. Sperm analyses were conducted at necropsy. Surviving F1 females were sacrificed on PND 42 and surviving F1 males were sacrificed on PND 49 unless they had not met criteria for vaginal patency or preputial separation, respectively.</p>
<p>Results</p>	<p>Maternal and Offspring NOAEL = 7500 ppm</p>
<p>Remarks</p>	<p>There were signs of a slight palatability problem with the 7500 ppm and 10,000 ppm diets with the males and the 10,000 ppm diet with the females as indicated by decreases in mean food consumption during the early part of the first week of the study. This problem resolved itself by the second week of the study. However, during the first week of gestation and for the entire postpartum period, mean food consumption was significantly decreased in the 10,000 ppm group females. There were no treatment-related clinical in-life observations, gross postmortem observations, or organ weight effect in the parental animals during this study. In addition, there were no statistically significant effects on reproductive indices or sperm parameters. The offspring displayed no treatment-related effects on survival, clinical observations, time to developmental landmarks, or offspring postmortem observations. Statistically significant suppression of body weight gain was observed in the 10,000 ppm adult females on PPD 4 and 14 when compared with controls. There were statistically significant decreases in the 10,000 ppm group's male mean offspring body weights on PND 14, 21, and 28. There also was a statistically significant decrease in the 10,000 ppm females' mean offspring body weight on PND 14 and 28. These decreases in body weight in dams and offspring were transient and were thought to be related to decreased maternal food consumption.</p>

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Conclusions	Under the conditions of this study Isooctanoic acid did not adversely affect reproductive parameters at doses that were nontoxic to the dams or their offspring.
Data Quality	1 - Reliable without restrictions
Reference	Exxon Biomedical Sciences, Inc. (1999) "One generation reproduction toxicity range-finding study in rats," Unpublished report.
Date last changed	August, 2001

Reproductive Toxicity

Test Substance CAS No.	Isononanoic Acid 3302-10-1
Method/Guideline Type of Study GLP Year	Other One-Generation Reproductive Toxicity Yes 1998
Species/strain Sex No. of animals/sex/dose Route of administration Dose/Concentration Levels Control group and Treatment	Rat/Sprague-Dawley Males and Females 10/sex/dose Dietary 0, 600, 1200, 2500, 5000 ppm in diet 10/sex
Statistics	For the statistical analysis the percent of normal sperm were transformed by Bloom's transformation. All variables were analyzed by standard one-way analysis of variance (ANOVA). Residuals from the model were tested for normality by the Shapiro-Wilk. When there were differences in-group means based on the ANOVA, differences in means were tested using Duncan's multiple range test.
Remarks on Test Conditions	P1 males and females (10 animals/sex) were exposed to the test substance for 10 weeks prior to mating. One male and one female were paired for up to 2 weeks. Beginning on GD 21, mated females were examined at least twice daily for signs of parturition. On PND 0, 1, 4, 7, 14, 21 and 28 the offspring were counted, sexed and each live pup was weighed. Pups were counted and examined externally on a daily basis during the postnatal period. On PND 4, after counting, weighing, and examining the pups, the size of each litter was adjusted by eliminating extra pups by random selection to yield as nearly as possible, 4 males and 4 females per litter. Pups from each litter were examined daily for developmental landmarks. Sperm analyses were conducted at necropsy. Surviving F1 females were sacrificed on PND 42 and surviving F1 males were sacrificed on PND 49 unless they had not met criteria for vaginal patency or preputial separation, respectively.
Results	Maternal and Offspring NOAEL = 1200 ppm
Remarks	<p>There were no treatment-related deaths or clinical signs noted in the parental animals during this study. There also were no treatment-related clinical signs noted for the offspring. There were no treatment-related effects noted for the male reproductive parameters such as sperm motility, total cauda sperm count, homogenization resistant spermatid count, sperm morphology, or the reproduction indices of mean male fertility, male mating, female fertility, fecundity, or gestational indices. In addition, there were no treatment-related effects on absolute or relative reproductive organ weights.</p> <p>In the 5000 ppm dose group, statistically significant decreases in parental food consumption were attributed to reduced palatability of the diet. Decreases in body weights were noted in the 5000 ppm females at Gestation Days (GD) 7 and 21 and at Postpartum Days (PPD) 4, 7, and 14. Mean absolute and mean relative liver weights were increased in both sexes of the 5000 ppm group.</p> <p>The offspring of the 5000 ppm group had reduced Live Birth Index and reduced survival indices on Day 1 and Day 4. Also, offspring body weights of both sexes were reduced during the postnatal period. Offspring body weight was also reduced in males and female of the 2500 ppm group.</p>

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Conclusions	Under the conditions of this study the test substance did not adversely affect reproductive parameters at doses that were nontoxic to the dams or their offspring.
Data Quality	1 - Reliable without restrictions
Reference	Exxon Biomedical Sciences, Inc. (1998) "One generation reproduction toxicity range-finding study in rats," Unpublished report.
Date last changed	August, 2001